DRG

ANNUAL REPORT

DIVISION OF RESEARCH GRANTS

FISCAL YEAR 1982

CONTENTS

HIGHLIGHTS

- Approximately 24,000 competing applications and 17,000 noncompeting applications received, processed, and assigned by the Referral Branch.
- Nearly 20,000 applications reviewed for scientific merit by Scientific Review Branch study sections.
- Over 52,000 requests processed by the Statistics and Analysis Branch through the IMPAC and CRISP computer systems.
- More than 13,000 information requests responded to by the Office of Grants Inquiries.
- Word processing capabilities of the Scientific Review Branch expanded. DRG Computer Resources Manual prepared, and training sessions organized to enable staff to use the Division's computer capabilities most effectively.
- Handbook for Referral Officers completed.
- Extramural data and trend publications prepared, including the Research Awards Index, Medical and Health Related Sciences Thesaurus, "Brown Book" series, and NIH Extramural Trends: 1972-1981 with accompanying slides.
- Research grant (PHS 398) and research grant continuation (PHS 2590) application kits revised. Research grant continuation kit and fellowship application kits (PHS 416-1, 416-9) redesigned from folders with inserts to self-contained booklets, consistent with the format of the PHS 398 kit.
- Division actively involved in two meetings held during February 1982 between the Chairpersons of NIH scientific review groups and key representatives of the NIH administration. Proceedings from these meetings published.
- Significant progress made in developing and implementing a data communications network utilizing remote terminals located in the various NIH extramural program offices.

OFFICE OF THE DIRECTOR

Dr. Carl D. Douglass, Director, discussed the NIH extramural program at meetings of the American Association of Medical Colleges in Washington, D.C., on October 7, 1981; the National Advisory Council of the National Institute of Dental Research, in Bethesda, Maryland, on January 26, 1982; the NIH Director's Advisory Council, in Bethesda, Maryland, on February 4, 1982; the Chairpersons of NIH Scientific Review Groups, in Bethesda, Maryland, on February 8 and 15, 1982; the University of Arkansas, in Little Rock, Arkansas, on February 16, 1982; the North Carolina State University, in Raleigh, North Carolina, on April 7, 1982; and the Association of Independent Research Institutes, in Miami, Florida, on September 17, 1982. Dr. Douglass was a member of the NIH Resource Allocation Group; Competitive Research Grants Program Policy Advisory Board, Department of Agriculture; Editorial Advisory Committee, American Men and Women of Science; NIH Coordinating Committee for Animal Welfare; NIH Animal Care Issues Committee; NIH Administrative Data Base Steering Committee; NIH Long-Range Facilities Planning Group; National Technical Information Services, Smithsonian Science Information Exchange Transition Committee, Office of Science and Technology Policy; and NIH Search Committee for the Director, Division of Research Resources.

Dr. S. Stephen Schiaffino, Deputy Director, discussed the NIH peer review process at the NIH Regional Seminar, "NIH Grants Administration," University of Kentucky, Lexington, Kentucky, October 21 to 23, 1981, and at the Society of Research Administrators Seminar, "Administration of NIH Grants," Monterey, California, May 5 and 6, 1982. Dr. Schiaffino also made presentations about peer review at two NIH meetings: at STEP Module III, held in Gaithersburg, Maryland, on February 17, 1982; and at a Grants Management Advisory Committee seminar, held in Bethesda, Maryland, on March 23, 1982. In addition, Dr. Schiaffino was a member of the NIH panel at a meeting of the National Council of University Research Administrators, in Washington, D.C., on November 5, 1981; and he participated in two meetings of the President's Cancer Panel--on March 29, 1982, in Boston, Massachusetts, and on June 22, 1982, in Westwood, California. Dr. Schiaffino was a member of the NIH group that visited the Medical Sciences Campus of the University of Puerto Rico on April 5 to 7, 1982 to discuss the NIH extramural program. Finally, Dr. Schiaffino was a member of the following NIH committees: Extramural Program Management Committee (EPMC); EPMC Task Force on Post-Investigational Sanctions; EPMC Subcommittee on Staff Development; Research Resources Coordinating Committee; Coordinating Committee on Manpower; BID International Representatives Committee; Subcommittee for Review of Division of Computer Research and Technology Central Services Financing; Subcommittee on Agency Management of Federal Radiation Research; Search Committee for the Deputy Director, Division of Extramural Affairs, National Heart, Lung, and Blood Institute; and Chairman, Search Committee for the Associate Director for Extramural Programs, National Institute of Dental Research.

Dr. Samuel M. Schwartz, Associate Director for Scientific Review, participated in the annual meeting of the National Council of University Research Administrators, in Washington, D.C., on November 5 and 6, 1981. In addition, Dr. Schwartz participated in the annual meeting of the American Society for Cell Biology, in Anaheim, California, on November 10 and 11, 1981 as a DRG representative. Dr. Schwartz was a member of the NIH Extramural Associates Review Panel, NIH Review Policy Committee, and NIH Consultant File Working Group.

Despite budget restrictions, the Division met the career development needs of many of its staff by again encouraging participation in some form of formal training. One hundred and ninety-one employees enrolled in job-related training courses, and 11 of them attended classes at the University of the District of Columbia as participants in the Upward Mobility Program.

The Division's Equal Employment Opportunity (EEO) program continued its efforts to promote equal employment for all employees--without regard to race, color, religion, sex, national origin, age or mental or physical handicap. A new EEO Counselor for the Division was appointed on December 14, 1981.

On January 20, 1982, the Employee Advisory Committee (EAC) held its first Open Forum. Employees were given an opportunity to meet EAC members and become knowledgeable of their functions and responsibilities. In addition, information was dispersed to the DRG staff from resource people representing the Employee Assistance Program, Career Development Program, Public Health Service EEO Office, DRG Personnel Office and Office of Worker's Compensation Program. A series of follow-up sessions is planned for the next fiscal year.

On March 12, 1982, a reception for Women's History Week was given for DRG staff by the EAC. Ms. Mattie K. Wright, Deputy Director for EEO, PHS, was the guest speaker. Ms. Wright discussed the federal women's role in promoting EEO programs.

One major activity this year was the desk-to-desk distribution of a questionnaire throughout the Division in an attempt to determine the problems and concerns of DRG employees. On March 16, the EAC met with the DRG Director, Deputy Director, Executive Officer, and Personnel Officer to discuss issues raised in the questionnaire. A summary of the discussion was published in the May 1982 issue of Keeping You Informed.

The Career Search Program was recently developed by the EAC and EEO offices. This program, to be implemented in the Fall of 1982, will provide short-term, on-the-job work experiences to DRG employees in offices outside of their normal work assignment.

EXTRAMURAL ASSOCIATES PROGRAM

Program Highlights

Twelve Extramural Associates from minority and women's institutions have been in residence and completed the Program during the current fiscal year. (See the attached listing of Associates.) The Associates completing residencies during fiscal year 1982 will bring the total since the Program began in 1978 to 44, representing 25 different states and territories.

Orientation and weekly scheduled seminars for fiscal year 1982 Associates (2 groups of 6 each) included a series of 102 lectures and conferences totaling 204 seminar hours. Seminars covered issues and topics pertinent to the NIH grant and contract processes; Bureau, Institute or Division (hereafter referred to as "Institute") intra- and extramural activities; and research programs of other Federal agencies.

Each group of Associates participated in a 5-day Congressional Operations Institute offered by the Government Affairs Institute, and made site visits to the National Institute of Environmental Health Sciences, the Environmental Protection Agency, and the Army Research Office, Department of Defense, at Research Triangle Park in North Carolina.

During this past fiscal year, Extramural Associates planned with their respective advisors and carried out 12 home institution site visits. These visits were to encourage increased and expanded utilization of the Associate's newly acquired expertise upon return to the institution following the NIH residency, and to review the institution's capabilities and research interests among faculty and administrators in order to guide and advise the Associate during the NIH residency.

The first Extramural Associates Program Workshop, jointly funded by participating institutions and the NIH, was held on June 30 to July 2, 1982, at the NIH campus. Overall attendance exceeded 80 persons, including Associates, advisors, and invited guests. With the theme of "More Research by Extramural Associate Institutions," the workshop focused on four major management areas: (1) future program direction, (2) role of Extramural Associate Program institutions in Federally funded research, (3) program evaluation, and (4) communications and information exchange. NIH Speakers included: Dr. James B. Wyngaarden, Director; Dr. William F. Raub, Associate Director for Extramural Research and Training; Dr. Zora J. Griffo, Special Programs Officer; Dr. Helen H. Gee, Chief, Program Evaluation Branch, Office of Program Planning and Evaluation; Mr. Storm Whaley, Associate Director for Communications; and Mrs. Barbara S. Bynum, Director, Division of Extramural Activities, National Cancer Institute.

During fiscal year 1982, the Program Director visited 13 colleges and universities in Delaware, Pennsylvania, New York, California, and Washington, D.C., to discuss with institution presidents, deans and top officials the requirements and objectives of the Extramural Associates Program. This approach has proven highly productive, for 50 percent of the candidates for the 1982-83 program year have been selected and scheduled to begin their residencies as the direct result of these visits. Twenty-one applications were received for the 1982-83 program year, and the 14 vacancies have been filled.

National publicity was carried out during fiscal year 1982 through the use of Extramural Associates Program exhibits displayed at conferences of the National Association for Equal Opportunity in Higher Education (NAFEO) held in Washington, D.C.; the Minority Biomedical Research Support Symposium, held in Albuquerque, New Mexico; the National Institute of Science and Beta Kappa Chi Scientific Honor Society, held in Washington, D.C.; and the North Carolina A&T State University Eighth Annual Symposium, held in Greensboro, North Carolina.

Program announcements for the 1982-83 program year have been mailed across the United States to over 300 administrators and scientists in colleges and universities that significantly contribute to the pool of minorities and women in science. Continuing communications among the NIH, Associates, and participating institutions were strengthened by distributing the second Extramural Associates Bulletin during the 1982 fiscal year.

Program Effectiveness

During the past fiscal year, all Extramural Associate institutions were asked to complete an information request describing the Associates' expanded responsibilities, development of research activities, dissemination of research information, and other research duties assumed since completing the Program.

Formal evaluation of the Program began in fiscal year 1982, and is being conducted by the Office of Program Planning and Evaluation, Office of the Director. Preliminary data indicate that approximately 50 percent of the Associates have been assigned expanded research responsibilities since completing an NIH residency, and over 75 percent of the Associates have been engaged in disseminating information acquired at NIH by conducting seminars and workshops regarding sponsored research.

Examples of individuals who have received new positions or have taken on additional research responsibilities since completing their Extramural Associate residencies include the following.

New Positions

- Dr. Edward G. High
  Meharry Medical College, Nashville, Tennessee
  Associate Dean for Basic Sciences

- Dr. Elizabeth J. Rock
  Wellesley College, Boston, Massachusetts
  Director, Office of Sponsored Research

- Dr. Marian Wilson-Comer
  Chicago State University, Chicago, Illinois
  Assistant to the Provost and Academic Vice President

- Dr. Willie J. Washington
  Central State University, Wilberforce, Ohio
  Director, Office of Faculty Development and Research

- Dr. Richie D. White
  Fort Valley State College, Fort Valley, Georgia
  Acting Coordinator of Research Administration

- Dr. Isabella N. Finkelstein
  Clark College, Atlanta, Georgia
  Chairperson, Biology Department

Additional Responsibilities

- Dr. John T. Hayes
  Paine College, Augusta, Georgia
  Director, Pre-Professional Science Programs

- Dr. Kinney H. Kim
  North Carolina Central University, Raleigh, North Carolina
  Coordinator of Research Activities

The Extramural Associates Program has developed high national visibility and is having significant positive impact upon the image and reputation of the NIH among institutions across the nation that contribute most to the pool of minorities and women in science and research. It is the intent of the Program to sustain and strengthen this trend.

NIH EXTRAMURAL ASSOCIATES PROGRAM

August 31, 1981 - January 31, 1982

Extramural Associates

Dr. Dorothy M. Feigl
Professor and Chairman
Department of Chemistry and Physics
St. Mary's College
Notre Dame, IN 46556

Dr. Franklin F. Flint
Professor and Chairman
Department of Biology
Randolph-Macon Woman's College
Lynchburg, VA 24503

Dr. Joseph L. Harrison
Professor and Chairman
Biology Department
Lincoln University
Lincoln, University, PA 19352

Dr. Virginia L. Martin
Professor of Biology
Biology Department
Queens College
1900 Selwyn Avenue
Charlotte, NC 28274

Dr. Mary E. McKelvey
Professor of Biology
Department of Biology
Fisk University
17th Avenue North
Nashville, TN 37203

Dr. Andrew B. Rudczynski
Assistant Director
Office of Research and Grants
University of Maryland, Eastern Shore
Princess Anne, MD 21853

Dr. Katherine L. Bick
Acting Deputy Director, NINCDS
Building 31, Room 8A52
496-3167

Dr. Thomas M. Valega, Chief
Restorative Materials Program
Branch, Extramural Programs, NIDR
Westwood Building, Room 506
496-7491

Dr. Dennis F. Cain, Chief
Grants Review Branch, NCI
Westwood Building, Room 820
496-7929

Dr. Constance W. Atwell, Chief
Strabismus Amblyopia and
Visual Processing Branch, NEI
Building 31, Room 6A49
496-5303

Dr. Bitten Stripp, Chief
Structure and Function Branch
Division of Lung Diseases, NHLBI
Westwood Building, Room 6A03B
496-7171

Dr. Anthony A. Rene, Chief
Office of Review
Activities, NIGMS
Westwood Building, Room 949
496-7585

NIH EXTRAMURAL ASSOCIATES PROGRAM

February 5 - June 30, 1982

Associates	Advisors
Dr. Kalyan K. Ghosh Executive Vice President and Vice President for Academic Affairs Shaw College at Detroit 7351 Woodward Avenue Detroit, MI 48202 (313) 873-0218	Dr. Robert Rabin Deputy Assistant Director for Biological, Behavioral, and Social Sciences Directorate, NSF 1800 G Street, N.W., Room 310 Washington, DC 20550 357-9894
Dr. Arthur J. Hicks Chairman, Department of Biology North Carolina A&T State University 312 North Dudley Street Greensboro, NC 27411 (919) 379-7907	Dr. Sara A. Gardner Program Director Pharmacological Sciences, NIGMS Westwood Building, Room 919 496-7181
Dr. Wilbert W. Johnson Chairman, Division of Natural Science and Mathematics St. Augustine's College Penick Hall of Science Raleigh, NC 27611 (919) 828-4451 ext 268	Dr. Ernest W. Johnson Diabetes Program Director Diabetes, Endocrinology and Metabolic Diseases Program, NIADDK Westwood Building, Room 628A 496-7348
Dr. Perry V. Mack Director of Development Associate Professor of Biology Bennett College Greensboro, NC 27420 (919) 274-6553	Dr. William E. Bennett Office for Research Manpower, NIAID Westwood Building, Room 7A03 496-5030
Dr. Linda H. Mantel Associate Professor of Biology City College of the City University of New York New York, NY 10031 (212) 690-8450	Dr. James F. Kavanagh Associate Director for Program Development Center for Research for Mothers and Children, NICHD Landow Building, Room 7C03 496-5097
Dr. Edward L. Risby Professor and Head Department of Biology Tennessee State University Harned Hall 3500 Centennial Blvd. Nashville, TN 37203 (615) 320-3322	Dr. William H. Goldwater Collaborative Programs Policy Officer, OERT, OD Building 1, Room 314 496-2241

GRANTS ASSOCIATES PROGRAM

The twentieth anniversary of the Grants Associates (GA) Program saw a reduction in the number of Grants Associates (the result of the hiring freeze) and a new look at how the Program might increase service to NIH during these times of constraints. In a Grants Associates Board position paper, which was presented to the Associate Director for Extramural Research and Training, NIH, and reviewed by the Extramural Program Management Committee, various options were suggested for meeting NIH's training needs for health scientist administrators. One option was to detail to the GA Program newly hired health scientist administrators and intramural scientists. The health scientist administrators would receive a varied and enriched training experience, while the intramural scientists would become a cadre of potential health science administrators for the Institutes. Other employees could also receive partial training to complement their experience sufficiently so as to permit their eligibility as health scientist administrators, thereby creating another pool of potential candidates for the Institutes. Plans for any changes in the Program are contingent on the recommendations of the Extramural Program Management Committee and the final decision by the Associate Director for Extramural Research and Training.

Six Grants Associates were in the Program this year, only three of whom entered the Program during the 1982 fiscal year. The others entered the Program during the last fiscal year but graduated September 30, 1982. Of the six Associates, one was female and two were minorities. Of the three who entered the program in fiscal year 1982, two were full-time, permanent PHS employees, and the third was an NIH staff fellow who was converted to a full-time, permanent position. Nine more selectees are available, but DRG's budget can permit a maximum of only five GAs in fiscal year 1983. Hence, for the time being, the Program has been reduced by 50 percent.

With the three graduates this year, each of whom took a health scientist administrator position at NIH, the total of GA graduates is 148: male, 126 (85 percent); female, 22 (15 percent); and minorities, 22 (15 percent).

There was an increase in the number of nominations to the GA Seminar Series this year (44) over last year (34). Because it was anticipated that the hiring freeze would reduce the number of GAs hired and therefore participating in the Series, the number of participants from among non-GAs was increased. Last year 17 were selected; this year 24 were selected. Selectees represented every Institute that nominated individuals for the Series.

As part of the 43 seminars in the Series, Dr. Edward Brandt, Assistant Secretary for Health, Public Health Service (PHS), Department of Health and Human Services (DHHS), presented a valuable overview of DHHS and PHS in the context of the current administration. In addition, a panel of speakers representing various roles in a university gave a seminar, which was followed by a

session from a program administrator. This seminar not only produced a lively exchange, but also provided the group with the perspectives and problems of university officials in extramural research and program administrators. The resulting dialogue enhanced communication and permitted mutual understanding of each other's problems. It also provided participants with practical information for any future encounters with principal investigators and university officials.

Three other new seminars were also added this year:

- Office of Prevention,
- International Activities, and
- NIH Data Systems.

Overall, the Series provided the group with a general understanding of DHHS and especially PHS, and with a broad perspective on the history and operations of the NIH and all of its components. All six PHS agencies were represented in the Series, as well as the Office of Management and Budget, the Office of Science Technology and Policy, the Office of Technology Assessment, the National Academy of Sciences, the National Science Foundation, and selected other offices within DHHS (e.g., Office of the General Council) and NIH (e.g., Office for Medical Applications of Research, Office for Protection from Research Risks).

This Seminar Series is a major portion of the formal training of Grants Associates. In addition, they are required to take five courses that are available to all Federal employees:

- The Introduction to Supervision,
- The Federal Budget Process,
- The Congressional Operations Institute for Managers,
- Management of Scientific and Engineering Organizations, and
- The Basic Project Officers Training Course.

Even with the amount of time required for these courses and the 172 hours for the Seminars, formal training consumed only 11.5 percent of the GA year. Hence, on-the-job experience remains the major form of GA training.

OFFICE OF GRANTS INQUIRIES

The Office of Grants Inquiries responded to more than 13,000 written and telephone requests for information on NIH extramural programs, research and training support mechanisms, and the peer review process. Congressional inquiries on these same subjects increased by at least 25 percent. Approximately 600 requests required either a manual search or a computer run on different research areas or disease entities, grantee institutions or principal investigators, and NIH support of Nobel Laureates and Lasker Award winners.

In addition, the Office was responsible for dissemination of information and applications for several special announcements, including a Request for Applications initiated by the Office of Adolescent Pregnancy Programs, Office of the Assistant Secretary for Health, PHS, the recently announced eligibility of for-profit organizations to apply for research grants, and the new administrative guidelines for the National Research Service Awards. These requests totaled 1,100.

The FASEB meeting, held on April 15-23 in New Orleans, Louisiana, generated close to 300 requests for publications on the NIH extramural programs and peer review from scientists attending the meeting. The Office cooperated with the NIH News Branch and DRG staff in providing informational material.

The Office also provided special data reports to DRG and the Office for Extramural Research and Training staff concerning responses to announcements on eligibility of for-profit organizations to apply for NIH grant support.

News releases were prepared on the annual listings of the NIH Grants and Awards and the Research Awards Index. Publications such as DRG Organizations and Functions, the Scientific Directory and Annual Bibliography, and the NIH Publications List were updated. The National Institutes of Health New Grants and Awards continued to be published quarterly for dissemination to the Congress, the press, and the general public. Several articles were submitted to the NIH Record, including those announcing the appointments of new Grants Associates.

Editorial services and assistance continued to be provided to DRG staff members preparing manuscripts for publication.

The number of visitors to the Office increased significantly this year, mostly as a result of the eligibility of for-profit organizations to apply for grants.

Graphic Arts

In fiscal year 1982, the Visual Information Specialist Office was relocated to the Grants Inquiries Office. As a member of the Office of the Director's staff, the Visual Information Specialist attended or participated in a number of meetings, presentations, and Division projects.

The Visual Information Specialist prepared or helped in the development of approximately 2,000 charts, tables, cover designs, photographs, certificates, flyers, viewgraphs, and layouts for publications. He also had about 1,000 slides duplicated at the NIH photography laboratory for presentations. In addition he coordinated work of a contractor (Creative Technologies Inc.) in preparing over 2,500 slides, prints, and other artwork for presentations both within and outside the NIH.

The Visual Information Specialist assisted in the development of visual materials for briefing packages for Dr. James B. Wyngaarden, Director, NIH. A current project is on the representation of women and minority scientists in research supported by the NIH.

OFFICE OF RESEARCH MANPOWER

Training Program Application Forms and Related Material

The revised individual fellowship application kits (PHS 416), both competing and noncompeting, should be in use by the end of the fiscal year. The numerous fliers and cards that accompany the application will be packaged as one unit thus saving assembly time before mailing. An optional computer prepared face page will be mailed to noncompeting applicants, saving them and NIH processing staff time on the printed items. Revised postdoctoral and senior fellowship announcements, which accompany the application, should also be available by the end of the year.

The revised institutional training grant application forms (PHS 6025), both competing and noncompeting, have been sent to the Office of Management and Budget for clearance. These forms were modified for use by all PHS training programs, thus eliminating the application forms PHS 2499-1 and -2.

A draft set of supplemental instructions allowing Research Career Development Award (RCDA) continuation applicants to use the standard PHS 2590 form is under development. This will eliminate the special form PHS 2557-2 and integrate the RCDA into the research grant mailing system.

Policy Development

A new guidelines brochure for the administration of National Research Service Awards (NRSAs) was issued June 18, 1982. This document, which replaced the July 1, 1976 guidelines, incorporated numerous changes made in the NRSA program especially involving payback requirements.

Review

A chapter on fellowship review has been prepared for the revision of the DRG Handbook for Executive Secretaries. In addition, a committee of fellowship executive secretaries has studied the review of foreign fellowship applications and has recommended changes to the Office of Extramural Research and Training, Office of the Director.

Information

The Office of Research Manpower continues to serve as a central information source on training programs for both the outside community and NIH staff. The latter is exemplified by staff serving on NIH-wide committees, such as the Training Budget Projections Committee and the NRSA Guidelines Revision Committee.

ADMINISTRATIVE BRANCH

The Administrative Branch continued to provide the Division with administrative and financial management, including budget and Scientific Review and Evaluation Awards, with property and supply control, and with space planning and assignment services; to maintain supplies of publications and application forms used in the PHS extramural programs; to be responsible for the efficient running of the components for effective coordination of procedures and services; and to maintain procedures for centralized distribution of application forms by the grantee institutions.

Financial Management Section

This Section assisted in administering about $22 million for the Division's operations, of which $17 million was from the NIH Management Fund, supplemented by $5 million from the Institutes for the support of Scientific Review and Evaluation Awards to initial review group chairpersons. The Section monitored expenditures from these funds through a computer database system that also provides NIH management with monthly, cost-analysis progress reports. As in the past, consultant costs were paid almost entirely from Scientific Review and Evaluation Awards, with consequent savings in both time and effort. The Section continues to report approximately 9,000 individual payments made to about 3,400 consultants, who submitted 7,200 vouchers to the NIH-wide, computer-based system for reporting consultants' incomes. In addition to the audit of the 7,200 consultants' vouchers, about 1,200 vouchers were audited by this Section for Division employees and others.

The Section prepared the Preliminary Estimate to DHHS, the OMB Submission, and the Manpower Submission for the Fiscal Year 1983 President's Budget, and also furnished information for the Fiscal Year 1982 Mid-Year Review. In addition, work has been started on the Fiscal Year 1984 Forward Plan. The Section continues to monitor the orderly flow of obligations and other aspects of budget execution as well as to respond to requests from the Division of Financial Management.

Office Services Section

This Section continued to review and approve requests for supplies and equipment needed by the Division, to provide property and supply control, and to participate in space planning and assignment. In its efforts, the Section accomplished a number of physical moves and planned several others, some of which were to accommodate the needs of several new study sections. The Section was also actively involved in the installation of IBM Displaywriters, which is the first phase of upgrading the quality of study section paperflow in the Scientific Review Branch. In addition, the Section has maintained the Division's Mail Room, and has been responsible for wide distribution of PHS

and NIH extramural forms and publications. The Section also continued to maintain liaison with other NIH service components for effective coordination of procedures and services, and to be responsible for supplying the control offices of the grantee institutions with application kits.

Previously a folder with various inserts, the research grant application kit (PHS 398) was changed by DRG staff last year into one self-contained booklet. This change not only improved its appearance, but also facilitated its processing by DRG staff, its distribution to applicants, and its completion by applicants. This year, three more kits have been converted to this convenient and highly acceptable format--those for continuation of research grants (PHS 2590), for individual fellowships (PHS 416-1), and for continuation of individual fellowships (PHS 416-9).

The number of grant application kits assembled and handled averaged around 10,000 a month, and about 9,500 miscellaneous packages were mailed each month. The Mail Unit received and processed approximately 41,000 grant applications of all types, as well as a large volume of supporting documents, letters, and publications.

Extensive technical contributions were made by staff in the development of several new and revised forms.

As noted in previous reports, the DRG Reference Room, which had been in operation for 20 years, was disbanded because of space and staff limitations. Reference materials continue to be decentralized into two basic locations, one housing texts and the other major reference books, such as Index Medicus and American Men and Women of Science. The Reference Committee continues to ensure the adequate provision of appropriate medical reference materials, and the Section remains extremely active in support of this activity.

REFERRAL BRANCH

Workload

The numbers of applications processed by the Referral Branch for this fiscal year are presented in Table 1. The Branch will have processed 23,559 competitive applications, which is a decrease of 12 percent from that of fiscal year 1981. Almost all of this decrease reflects applications submitted for the last two National Advisory Council and Board rounds. In addition, the Branch will have processed 17,083 noncompetitive applications. Figure 1, which is a workload profile for the Referral Branch, places fiscal year 1982 in perspective.

Six computer terminals, recently installed in the Project Control Section, are being used by staff to enter records directly into the IMPAC system for competing grant applications. A computer print-out is to be provided on a daily basis. Programming for identity of those applications whose assignments have been changed is underway. When this is developed and assurance of a daily computer print-out (update) can be obtained, this can substitute for the Branch's present card file system, with a subsequent saving in staff time.

Two changes in procedures have resulted in a significant impact on staff time. Of greatest impact has been the change in handling the distribution and printing of applications. The original is no longer sent to the print shop, but is forwarded directly to the Institute, and a copy of the original application is now used for duplication purposes by the Print Shop. Thus staff no longer need to reassemble the original application upon return from the Print Shop before forwarding it to the awarding unit to become a part of the official file. This procedure not only saves staff time, but also allows the awarding units to set up official files and inform program staff about assigned applications in a more timely fashion. In a second procedural change, "pulling" investigator records (microfiche) for noncompeting applications has been discontinued. The small number of these applications that do not conform to the computer records are expected to be identified by rejection by the computer, and where the changes have not been recorded in the computer, they are expected to be identified by Grants Management staff.

Staff Activities

A new Referral Officer (Dr. Willard McFarland) was recruited to replace one who retired (Dr. William Morris).

In the Project Control Section, Ms. Vernita Dawkins served on the NIH Women's Advisory Committee.

Ms. Christine Miles participated in the NIH Career Education Program. She earned an additional 4 credits towards the development of skills in business management.

Branch Documents

The Branch developed, for internal use only, a reference handbook consisting of guidelines and associated materials for making assignments to review committees within the awarding units.

TABLE I

APPLICATIONS PROCESSED BY THE REFERRAL BRANCH IN FISCAL YEAR 1982

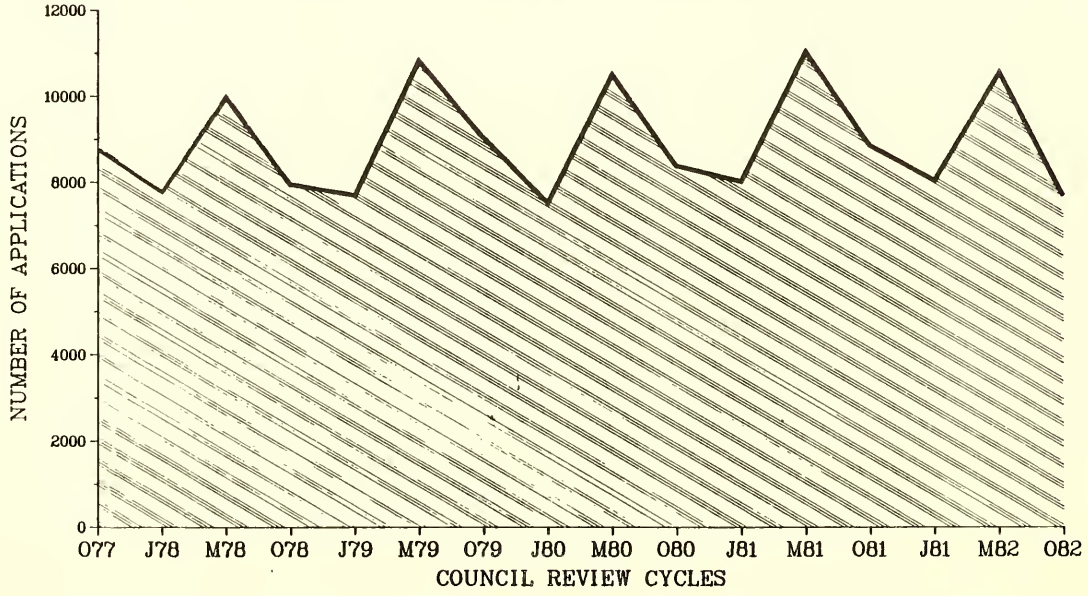
Council		May 1982	October 1982	January 1983
Receipt Date		Oct-Nov 1981	Feb-March 1982	Jun-July 1982 *
			COMPETING	
Number of Applications	New	7167	5149	
	Renewal	2727	1776	
	Supplement	142	98	
	TOTAL	10036	7023	6500
Activities	R	8269	5902	
	T	432	123	
	F	1033	774	
	K	274	150	
	Other	28	74	
Distribution (percent)	NIH	89.0	90.5	
	ADAMHA	9.8	8.5	
	Other	1.2	1.0	
			NON-COMPETING **	
Type 5		4754	5183	5904
Interim (administrative)		550	281	411 ***
	TOTAL	5304	5464	6315

* Estimated numbers since report prepared prior to end of FY year.
** Non-competing applications are received each month. Figures for Type 5 applications reflect the interval from one Council round to the next.
*** Figures reflect activity through July only.

5/19/82

FIGURE 1

REFERRAL BRANCH
COMPETITIVE APPLICATIONS PROCESSED



JL22 5/19/82

FINAL DATA. INCLUDES WITHDRAWALS PRIOR TO REVIEW.
DEFERRALS ARE COUNTED TWICE.

RESEARCH ANALYSIS AND EVALUATION BRANCH

The Research Analysis and Evaluation Branch continues to serve as a staff resource to the DRG and NIH directorates in the development and preparation of reports on selected biomedical fields, and to engage in various tasks or projects to aid in the administration of the NIH extramural programs. In cooperation with the Scientific Review Branch, the Research Analysis and Evaluation Branch completed a study analyzing the initial review of applications to conduct clinical research. Staff prepared a comprehensive report that summarized and compared previous studies, and also included a new research effort to assess the reasons for poor ratings or disapprovals of clinical research and development grant applications. Based on the latter part of the report, the Branch submitted an article for publication in Science. The study showed that clinical research project applications do not fare as well as those that do not involve human subjects; but the pattern of shortcomings, principally in the area of technical methodology, is similar to that seen in basic research and other nonclinical applications.

The Branch partially updated studies on the rates of entry and characteristics of new principal investigators to include actions through fiscal year 1980. Analyses emphasizing relationships between support of principal investigators and prior NIH-sponsored research training have been facilitated by the data resources created in cooperation with the Statistics and Analysis Branch of DRG and the National Research Council. In response to the increasing number of inquiries from the Institutes regarding the use of these data to evaluate their activites, Branch staff assisted Institute personnel by making data available and by sharing methods developed in the Branch.

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases intends to use a methodology developed in the Branch to automate the classification of research and development grants and contracts in order to prepare required annual reports to the National Science Foundation and to the Office of Management and Budget. Branch personnel participating in the joint project are working on improvements in the method based upon an adaptation of the DRG CRISP (Computer Retrieval of Information on Scientific Projects) system to broader concepts of basic and applied research. Other Institutes have also expressed interest in testing this methodology for their own purposes.

During the past fiscal year, several analyses in such areas as the NIH support of research in the psychological and social sciences, physical sciences, and pharmacology, as well as kinds of research animals, health services research, and clinical trials, were the basis for reports or presentations. A National Research Council resident fellow has been assigned to do a study that examines the role of chemistry programs (including biochemistry and clinical chemistry) in supporting the health research mission of the the NIH. A central point of contact for the resident fellow's use of NIH data resources has been the Research Analysis and Evaluation Branch.

Branch staff represent the Division in a number of committees, including those for clinical trials, the Office of the Medical Applications of Research, animal resources, disease prevention and health promotion, behavior and health research, Federal agency chemistry programs, legislative analysis, activities of planning and evaluation officers, and NIH reporting of research and development to the National Science Foundation.

The Chief of the Branch participated in a meeting sponsored by the National Council of Drugs, and presented data on the NIH support of pharmacology research and on the entry of new principal investigators into the NIH research grant system. In addition, the Branch Program Analyst presented a study on the initial review of clinical research grant applications to the Associate Director for Extramural Research and Training, NIH, and his staff.

SCIENTIFIC REVIEW BRANCH

The workload continued to be heavy, with the Branch reviewing 19,783 competing applications. The major thrust of the 1982 fiscal year effort was toward the twofold, interrelated objectives of strengthening management capabilities and improving the quality of the peer review by the study sections. The items reported below are related to attaining these objectives.

The Branch's word processing capabilities were greatly expanded. By the end of this fiscal year, 28 IBM Displaywriters were in place, 8 of which were equipped with modems to allow the word processors to interact with the NIH computer systems. This interactive capability has enabled Grants Assistants to access the computer for mailing labels, lists of reviewers, and other aids that will increase the efficiency of office procedures. In addition, Executive Secretaries can access data banks in order to identify consultants for the study sections. In collaboration with the Statistics and Analysis Branch, the Scientific Review Branch prepared a DRG Computer Resources Manual and organized training sessions for staff to enable them to use the Division's computer capabilities most effectively.

Additional training sessions for staff and consultants were planned. Committees are developing an orientation program for new members of study sections as well as training programs for Executive Secretaries and Grants Assistants.

All instructional materials for consultants have been updated to incorporate, among other issues, the new regulations concerning human subjects involved in research and a more detailed documentation of the review of vertebrate animals used in research. Related to the updates, the Handbook for Executive Secretaries is being revised, and NIH Peer Review of Research Grant Applications, the booklet accompanying the Branch's extensive, ongoing slide collection, was updated.

Finally, Branch staff were actively involved in revising the various application packets used by the scientific community. The research grant application kit (PHS 398) and the instructional booklet for a Research Career Development Award were updated; and the research grant continuation (PHS 2590), individual fellowship (PHS 416-1), and individual fellowship continuation (PHS 416-9) application kits were revised and reformated into single booklets, consistent with that of the PHS 398.

Staff evaluation procedures continued to involve considerable time and effort on the part of all Branch personnel. The merit pay plan that was developed during the 1981 fiscal year was successfully implemented, but needed to be modified in the 1982 fiscal year to meet changing NIH policy. In addition, a committee developed an Employee Performance Management System (EPMS) plan for Grants Assistants. As with the merit pay plan, the Committee prepared detailed evaluation standards and procedures that were consistent with the NIH guidelines and yet relevant to the special needs of the Branch.

The Branch also actively participated in the most recent series of meetings between the chairpersons of the NIH scientific review groups and key representatives of the NIH administration. For these two meetings, which were held during Feburary 1982, the attending chairpersons were from review groups not represented at the 1981 meetings. The Office of the Associate Director for Scientific Review prepared the Proceedings, which merged the group discussions and individual presentations from the meetings into one compact volume.

Workshops or Symposiums Sponsored by Study Sections

In conjunction with its March 1982 meeting, the Allergy and Immunology Study Section held a seminar on the topic of "Recombinant DNA Technology in Immunogenetics and Immunochemistry." Dr. Malcolm Gefter of MIT was an invited speaker. Discussion centered on a comparison of recombinant DNA (genetic) approaches and protein sequencing approaches to determining the structure of immunologically important molecules.

The Epidemiology and Disease Control Study Section, in conjunction with its June 1982 meeting, held a workshop dealing with peer review at the NIH. Dr. Ann Schluederberg and Dr. Michael Alavanja made presentations concerning DRG and Epidemiology and Disease Control Study Section trends in approval rates and priority scores. Other topics that were discussed included alternative methods for calculation of priority scores and ideas for mini-scientific workshops to be conducted in conjunction with regular study section meetings.

In conjunction with its regular spring meeting, the Nutrition Study Section sponsored a workshop on Nutrition and Endocrine Disorders. This workshop, on June 11, 1982, was held in cooperation with the Western Human Nutrition Center, U.S. Department of Agriculture (USDA). Invited speakers were Drs. L. Salans (NIH), O. Owen (Temple University), R. Anderson (USDA), J. Hirsch (Rockefeller University), G. Reaven (Stanford University), and M. Greenwood (Vassar College). Approximately 55 scientists attended, including some in attendance at the annual meeting of the American Diabetes Association.

The Reproductive Biology Study Section sponsored a workshop on "The Role of Peptides and Proteins in Control of Reproduction." This workshop was held in Bethesda, Maryland, on February 15-16, 1982, in conjunction with the Study Section meeting. Recently, rapid progress has been made in the area of potential control for fertility by the use of one or several peptides that control reproduction. The purpose of the workshop was twofold: first, to serve as an important educational vehicle for Study Section members who are not working directly in this field; and second, to assess the potential application of peptides in fertility control. Seventeen speakers provided scientific papers, followed by extensive discussion. Approximately 250 scientists, including Reproductive Biology Study Section members, attended the workshop. The proceedings of the workshop are being published by Elsevier North Holland, Inc., New York.

Professional Activities

During the fall of 1981, Dr. Michael Alavanja, Executive Secretary, Epidemiology and Disease Control Study Section, lectured on the use of "Epidemiology in Quantitative Risk Assessment" in conjunction with a course entitled "Quantitative Risk Assessment" sponsored by the NIH Graduate School. He also presented a seminar on "Quantitative Risk Assessment" at the Graduate School of Health Science at Hunter College of the City University of New York on May 6, 1982. Dr. Alavanja also peer reviewed two manuscripts dealing with environmental epidemiology for the Journal of Environmental Health.

Dr. Harry J. Brodie, Executive Secretary, Physiological Chemistry Study Section, participated in and chaired a session at a workshop in Key Biscayne, Florida, from December 6 to 9, 1981, on "Aromatase: New Perspectives for Breast Cancer." Dr. Brodie also reviewed a grant application for the Medical Research Council of Canada.

Dr. Dharam S. Dhindsa, Executive Secretary, Reproductive Biology Study Section, reviewed three manuscripts for the International Goat and Sheep Research Journal, and reviewed two research proposals for scientific merit for the National Science Foundation. He also served on the Membership Selection Committee for 1981-82 for the Society for the Study of Reproduction. Finally, Dr. Dhindsa represented the NIH at the Annual Meeting for the Gynecologic Society in Dallas, Texas.

On April 5, 1982, Dr. Martin Frank, Executive Secretary, Physiology Study Section, presented a seminar entitled "NIH Peer Review and Research Funding Mechanisms" to the Department of Physiology and Biophysics, University of Illinois College of Medicine, Chicago, Illinois. During this past fiscal year, Dr. Frank was also Associate Professorial Lecturer, Department of Physiology, the George Washington University School of Medicine, Washington, D.C., and a member of the Research Committee, American Heart Association, Nation's Capital Affiliate.

Dr. Clarice E. Gaylord, Executive Secretary, Pathobiochemistry Study Section, represented DRG at the North Carolina A & T Extramural Funding Symposium, held on December 2 and 3, 1981, in Greensboro, North Carolina.

During the last fiscal year, Dr. Arthur S. Hoversland, Executive Secretary, Human Embryology and Development Study Section, reviewed 26 scientific manuscripts for publication in refereed journals.

Dr. Asher A. Hyatt, Chief, Biomedical Sciences Review Section, acted as one of the facilitators for NIH STEP Module III, "Creative Response to Changing Demands: Peer Review of Grant Applications," in February 1982. In February, Dr. Hyatt also ran an all-day NIH Grantsmanship Workshop at the University of Nebraska Medical Center, Omaha. During this fiscal year, Dr. Hyatt again chaired the Form PHS 398 Revision Committee. Its task was completed and the new form has now been printed.

Dr. Miriam F. Kelty, Chief, Behavioral and Neurosciences Review Section, serves in a variety of governance positions in the American Psychological Association. During 1981 she chaired the Public Information Committee of the Division of Health Psychology and was charged with getting a new journal started. At the same time, she has been on the Fellowship Committee, the Committee on Women and Health, and the Legislative Forum. As Past-President, she is a member of the Board of Directors of the Division of Psychologists in Public Service, the Division's Recognition Awards Committee, and the Membership Committee, and represented the Division on the Association's Council of Representatives. She is also an active member of the Division of Population and Environmental Psychology, the Division of Comparative Psychology, and the Division of the Psychology of Women. Dr. Kelty is an invited member of the Washington Area Bioethics Seminar, an ongoing seminar of individuals from area academic institutions, Government agencies, Congressional committees, public interest groups, the religious community and the journalist community that meets monthly to discuss ethical issues in science and technology and their implications for society. She is also an invited participant in the Health Policy Forum, an ongoing series of seminars and workshops on health policy issues attended by Congressional staff and agency personnel. From September 1981 to March 1982, Dr. Kelty served as a consultant to the National Academy of Sciences, Institute of Medicine's Committee on Research in the Assessment of Birth Settings, contributing to the Committee in the area of psychosocial factors. On October 19 and 20, 1981, Dr. Kelty, as an American Psychological Association Distinguished Visitor, presented a seminar at S.U.N.Y. at New Paltz on ethical responsibilities of researchers. She also met with students and faculty for informal sessions on research review and human subjects policies. On November 12, 1981, Dr. Kelty participated in a symposium on Federal Support of Research at the Psychonomic Society's meeting in Philadelphia. On December 2 to 4, 1981, she provided information about the nature and scope of research support available from the NIH at the Washington, D.C. meeting of the Council of Graduate Schools in the United States. From December 1981 through May 1982, Dr. Kelty was a member of the Planning and Organizing Committee and a referee for papers for the World Future Society's International Congress on Communications and the Future. In February 1982, Dr. Kelty prepared a detailed critique of the draft volume, Ethical Principles in the Conduct of Research with Human Participants, for the Committee on the Protection of Human Subjects of the Board of Scientific Affairs of the American Psychological Association. On March 11, 1982, she participated in seminars on information systems at the Federal Office Systems Exposition. On April 19, 1982 she attended a symposium on Mental Health in China. From April 20 to September 1982, she served on the editorial board for the Institutional Review Board Guidebook being prepared by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. On April 27, 1982, Dr. Kelty represented the Division at the Cognitive Science Consortium, an informal interagency group of those involved in support of cognitive and other behavioral research. On June 17 to 19, 1982, Dr. Kelty spoke at a workshop on Institution Review Boards designed to educate members of those boards about current policies and practices. On August 22 to 25, 1982, Dr. Kelty participated in scientific symposia on the American family, in a policy-oriented symposium on peer review, and in several Executive Committee, Board and Council meetings in conjunction

with the Annual Meeting of the American Psychological Association. Dr. Kelty has just completed a 6-year editorial term for the Journal of Population and Environment and is a consulting editor of Health Psychology.

On April 16, 1982, Dr. Lottie Kornfeld, Executive Secretary, Immunological Sciences Study Section, presented a seminar entitled "Your Grant Application to NIH" at the Department of Microbiology, George Washington University School of Medicine, Washington, D.C.

At the annual meeting of the American Orthopsychiatric Association, held in San Francisco, California, from March 29 to April 2, 1982, Dr. Teresa E. Levitin, Executive Secretary, Human Development and Aging Study Section, organized and chaired a paper session entitled "Mediation: Assumptions, Approaches, and Outcomes." Dr. Levitin also spoke on the "Influence of Parental Work Patterns on Family Styles and Child Outcomes" and acted as a discussant during a paper session entitled "Children of the Children of the 60's: A Longitudinal Perspective." At the annual convention of the American Psychological Association, held in Washington, D.C., from August 23 to 27, 1982, Dr. Levitin presented two papers--"Overview of the Review Process" and "Child Health Research Priorities"--for a symposium on "ADAMHA-NIH Support for Behavioral Science Research." In addition, Dr. Levitin was a discussant on a symposium called "(Re)Defining Social Problems--Divorce: From Problem to Opportunity." Throughout the fiscal year, Dr. Levitin was a member of the Steering Committee of the Society for the Advancement of Social Psychology, the Executive Board of the Family Mediation Association, and the Editorial Review Board of both the Journal of Social Issues and the Journal of Family Issues.

Dr. Betty June Myers, Executive Secretary, Tropical Medicine and Parasitology Study Section, was Associate Editor of the American Society of Parasitologist Newsletter and a member of the Membership Committee of the American Society of Tropical Medicine and Parasitology.

From November 9 to 13, 1981, Dr. Ramesh K. Nayak, Executive Secretary, Molecular Cytology Study Section, attended the Annual Meeting of the American Society of Cell Biology, in Anaheim, California. At this meeting, Dr. Nayak participated in staffing the NIH booth and answering questions from investigators regarding peer review at the NIH as well as policies and procedures for submitting grant applications.

Dr. Antonia C. Novello, Executive Secretary, General Medicine B Study Section, received a Masters Degree in Public Health, with a concentration in health science administration, from the Johns Hopkins University School of Hygiene and Public Health in May 1982. During the past fiscal year, Dr. Novello was also a member of the Committee on Research in Pediatric Nephrology, American Society of Pediatric Nephrology; a representative on the NIH Task Force Site Visit Team, University of Puerto Rico (April 1982); and Co-chairperson of the Third International Congress on Nutrition and Metabolism in Renal Disease, at Marseilles, France (September 1 to 4, 1982). Dr. Novello presented scientific papers on "Pediatric Nephrology Applications Revisited," at the Annual Business Meeting, American Society of Pediatric Nephrology, Washington, D.C., on May 13, 1982; and on "The M.D. as a Competitive Investigator," at the Childrens

Hospital National Medical Center, Washington, D.C., on June 17, 1982. Finally, Dr. Novello gave a course on Pediatric Nephrology, as an Associate Professorial Lecturer, for the Department of Pediatrics and Ministry of Health, Bogota, Columbia, from September 28 to 30, 1982.

On June 1, 1982, Dr. Samuel C. Rawlings, Executive Secretary, Human Development and Aging Study Section, spoke on "The Proposal Review Process" and served on a panel with several researchers and academicians addressing questions on this topic. This occurred during an all-day workshop entitled "First Steps to a Scientific Career," held at the University of Illinois Medical Center. Dr. Rawlings also gave a presentation on "The NIH Review Process from the Perspective of an Executive Secretary" at an all-day workshop entitled "Gerontology in Aging Research," sponsored by the American Psychological Association, on August 22, 1982.

Dr. Ann Schluederberg, Executive Secretary, Epidemiology and Disease Control Study Section, participated in a workshop, "NIH and Physical Anthropology: Grants Application and Peer Review," held at the American Association of Physical Anthropology meeting, on April 1, 1982, in Eugene, Oregon. She also served on the Scholars' Advisory Board of the Fogarty International Center and as a reviewer for the Journal of Infectious Diseases.

From January 26 to 28, Dr. Thomas M. Tarpley, Executive Secretary, Oral Biology and Medicine Study Section, gave a course on "Submitting Successful Research Proposals" for the Continuing Education Program of the University of Puerto Rico. Dr. Tarpley also gave the following lectures or seminars: "CPC's-Mock Board Examination," AFIP, October 1, 1981; "Research Grants: How to Hang Your Stocking and Decorate the Tree," University of Minnesota School of Dentistry, Special Seminar, December 18, 1981; "Non Neoplastic Salivary Gland Lesions," National Naval Dental Center Continuing Education Course in Oral Pathology, Bethesda, Maryland, January 19, 1982; "Salivary Gland Diseases," Oral Pathology, Armed Forces Institute of Pathology, Washington, D.C., March 11, 1982; and "Intravascular Fibramatosis," Special Seminar, "Dog Tumors: Similarity to Human Tumors," and "Abnormal Presentation of Basal Cell Carcinoma," AFIP/AAOP, Reno, Nevada, May 2 to 5, 1982.

During this past fiscal year, Dr. Adolphus Toliver, Executive Secretary, Biochemistry Study Section, received an NIH Award of Merit and also an award for "Outstanding Service to Biochemical Research" at the annual meeting of the American Society of Biological Chemists in New Orleans, Louisiana (April 19, 1982). Dr. Toliver presented seminars on the "NIH Peer Review: A Study Section Perspective" at the West Central States Biochemistry Conference, University of Nebraska, Lincoln, Nebraska, October 15 to 17, 1981; at the Division of Neuropathology, School of Medicine, University of Pennsylvania, January 13, 1982; and at the School of Medicine, University of Miami, Miami, Florida, February 3, 1982.

Dr. Eugene M. Zimmerman, Executive Secretary, Allergy and Immunology Study Section, served on the Faculty for STEP Module I, "Introduction to Extramural

Programs," on December 8 and 9, 1981. He was involved with the sections dealing with the initial review of grant applications and the review of contract proposals.

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STATISTICS AND ANALYSIS BRANCH

The Statistics and Analysis Branch (SAB) is involved in almost every facet of NIH's extramural activities. Through its IMPAC System (a cental data system on extramural activities), the Branch performs services at virtually every stage of application processing, from initial receipt through the final award. SAB assists the Referral Branch by providing every 2 weeks a microfilm containing information on all applications, awards, and contracts recorded in the system, and the Scientific Review Branch by providing various documents, such as the Resume of IRG Actions and the form for application summary statements ("pink sheets"). In addition, SAB assists the National Advisory Councils and Boards (or Councils) as well as the awarding units, by providing such services and documents as the Resume of Council Actions and the Notice of Award.

While providing these services, the Branch develops a data base on the extramural activities of the NIH. These data are used to support all levels of NIH management and to provide a source from which NIH can meet its reporting obligations.

SAB also operates CRISP (Computer Retrieval of Information on Scientific Projects), a sophisticated computer disk storage and retrieval system. CRISP maintains scientific information, under approximately 7,900 subject headings, on all PHS-supported research projects by fiscal year starting from fiscal year 1971.

Through its two major information systems, IMPAC and CRISP, and other small systems, such as the Committee Management System, Trainee Appointment File, NRSA Payback File, and Institution Profile File, SAB provides information services on extramural programs to all levels of management, other Government agencies, and the public.

During the past year, the Branch made significant progress in developing and implementing a data communication network utilizing remote terminals, which were installed in various NIH extramural offices. The new network system ties together the receipt and processing of applications in the Referral Branch, the preparation of worksheets, pink sheets, and resumes in the initial review groups, and the preparation of award statements and associated documents within the funding Institutes. It is expected that full implementation of the new integrated network system will not only result in significant manpower savings but also greatly improve the quality and timeliness of information recorded in the IMPAC system.

1. Systems and Data Management Section

a. Automated Logging System

An automated system for the assignment of grant application numbers and source document data capture is fully operational in the Project Control Section, Referral Branch. Through an interactive computer program, all competing grant applications are now processed through this system.

The Project Control staff enter a minimum of five data items on computer terminals, after which the system assigns a number and generates a series of labels for each application. These labels eliminate much of the workload of the Project Control staff by automatically preparing (1) information required by the Print Shop for multiple copies of the application, (2) information for the distribution of copies to appropriate Institutes and initial review groups, and (3) information required by the staff for logging and indexing. Computer-generated data guarantee swift and accurate processing of the necessary forms. In addition, the system provides the necessary data to establish a skeleton record in the IMPAC file.

b. Application-Grant Status File

SAB is currently designing a system to facilitate the processing of official changes to applications and grants. Under the present system, the administering Institute or initial review group must complete a 901 form, sending copies to the concerned units. Upon receipt of the 901 form, the Data Control Unit, SAB, changes the IMPAC record and issues the Resumè of Transactions report, which is then distributed throughout the NIH advising of the change.

The new system will accomplish the same functions through an interactive computer program. The program will prompt the user to insure the integrity of the data being recorded and will request additional information when appropriate. Changes to the IMPAC record and Resumè of Transactions report will be on a daily basis. The system will be implemented in two phases: the first phase will accommodate changes made through the Project Control Section; and the second phase will respond to changes initiated by the Institutes.

c. Enhanced Storage

The IMPAC and CRISP systems' on-line files were converted to the newly installed IBM 3380 disk storage devices supplied by the Division of Computer Resources and Technology. These higher density storage devices provide greater data storage in less space as well as accelerated access time to the data, resulting in increased efficiency of operation.

d. Workload Reports

A Workload Report File has been established, which is maintained online for daily updating. Information is organized by Council date for each initial review group. Applications received and processed are totaled by NIH Institutes as well as by non-NIH administering organizations.

e. Council Notification Procedure

A new procedure has been established through which Council recommendations are supplied to the Institutes for recording purposes by means of reports that list all applications received, including initial review group recommendations. The information can be provided in various sorting arrangements, such as by program, application number, or investigator.

f. Flexible Initial Review Group Designator Code

A new item has been established in the IMPAC system to indicate subgroupings within an initial review group, when appropriate, to produce separate work documents such as worksheets, resumés, summary statements, and summary statistics for each of these subgroups.

g. IMPAC Reconciliation with NIH Central Accounting System (CAS)

A new computer program automatically compares accounting data in the CAS with similar information in the IMPAC system. Differences between amounts awarded and amounts encumbered are examined, and, as necessary, updates are made to the IMPAC and/or CAS system. This procedure will ensure compatibility of the two systems by resolving errors on a weekly basis throughout the fiscal year.

h. Interactive Awards and Obligation Procedures

An interactive computer program now allows for the preparation of award statements within the Institute offices. With this program, Institute staff can prepare awards through their own CRT terminals and printers, and the program prompts for all the items appearing on the Notice of Grant Award. Currently, 50 percent of the NIH Institutes and one ADAMHA awarding unit have been trained in and are using the system; the other Institutes will soon be trained or are awaiting the acquisition of terminals and printers. A program is also being developed for preparation of the Notice of Research Fellowship Award.

i. DRG Personnel Information System

With the newly designed DRG Personnel Information System, staff have fast access to a variety of data, including the pending,

current, and future status of DRG employees. The system calculates hours worked, projected hours for the year, and full-time equivalencies, and tracks pending actions. In addition to providing standard reports by organization, and status codes, the system is accessible via an interactive query. Through this mechanism, data may be obtained according to any criteria specified by the user.

j. Priority Score Computation

An interactive module has been developed to record the recommendations of each reviewer. These data are then used to compute the initial review group's priority scores. With this module, the efficiency of processing is increased, and the possibility of error is substantially reduced. The system will be expanded to include recording the dollars recommended by each member of the initial review group and transferring the information directly to the IMPAC system.

k. Computer Retrieval of Information on Scientific Projects (CRISP)

The CRISP system files have been restructured. The change halved the amount of storage used by this large data base and also reduced significantly the amount of computer time required to retrieve information.

l. National Research Service Award (NRSA) Payback

Through a major redesign, the provisions of the Omnibus Reconciliation Act of 1981 were incorporated into the NIH system. The new law eliminates the initial 12 months of NRSA support from computation of the payback obligation, and covers all recipients in training on that date, as well as all recipients of awards made prior to its enactment who had not begun or who were in process of fulfilling the payback obligation. All records on file were adjusted according to individual circumstances. These provisions do not apply to individuals in delinquent payback status prior to the enactment date.

2. Research Documentation Section

The Research Documentation Section maintains the CRISP system, which contains scientific data on research grants, contracts, and cooperative agreements supported by the PHS and NIH, as well as National Institute of Mental Health intramural research projects. Through this system, the Section responds to requests for scientific information from Government administrators, scientists, and information personnel to evaluate research programs or specific scientific areas, or to prepare reports. Similarly, the Section responds to inquiries from grantee and non-grantee institutions, scientists, the news media, and other non-Government sources engaged in, concerned with, or reporting on medical research.

Annual publications from CRISP include:

- The Research Awards Index, prepared in two volumes. Volume I is a scientific subject index with associated project numbers and titles. Volume II contains project identification data, research contract identification data, and project principal investigator information; and

- The Medical and Health Related Sciences Thesaurus, the vocabulary authority list of subject headings used by the Section staff in indexing research projects. The Thesaurus is available for Departmental use only.

CRISP has the query capability of (a) providing, in several optional formats, information ranging from a straightforward listing of research pertaining to a single scientific subject term to a compendium of projects relating to any number of terms; (b) furnishing individual Institutes with tapes or hard copy of their projects by subject, project, subproject, title or name of investigator; and (c) generating institution and Institute listings of projects with indexing terms (Scientific Profiles). CRISP also has the query capability of limiting subject searches or Scientific Profiles to certain program activities or Institution Profile File (IPF) codes.

A specially designed CRISP subroutine can supply grantee institutions or Institutes possessing appropriate computer capabilities with specially formatted tapes, which they can use to search the scientific subject content of their own research grant and contract records. It can also provide NIH program staff with similar tapes of project records pertaining to selected scientific areas. This subroutine, called CESI (CRISP Extract System for Institutions/Institutes), is updated monthly and can furnish selected tapes on an ad hoc or recurring basis.

a. Subproject Information

A significant feature of the CRISP system is its capability of subdividing program projects, centers, and other large projects into their individual research components, thereby providing detailed and accurate information on the research objectives of these large grants as well as the names of principal investigators conducting the research.

b. CRISP Services

During the past fiscal year, the Section responded to over 1,400 requests on a wide range of subjects; provided Scientific Profile data reports and/or CESI tapes for grantee institutions; furnished NIH-wide scientific area data for appropriate Institutes; and performed professional editing operations involving thousands of approved research grant and contract applications. In addition, the Section played a significant role in providing or updating material on various trans-NIH issues.

c. Intramural Research Projects

Professional indexing and entry into CRISP of scientific keyword, title and principal investigator data from fiscal year 1981 intramural research projects were completed soon after receipt of the last annual report in November. This information was subsequently published in the annual NIH-NIMH Intramural Research Index, which was distributed in May.

d. Research Awards Index (NIH Publication No. 82-200)

Response to the NIH appeal granting permission to distribute gratis copies of the Index to biomedical libraries was received in late June, delaying the expected publication date until August. Meanwhile requests for these popular volumes and letters expressing concern regarding their continued availability have been pouring into the Section.

e. On-Line Access

Use of the CRISP System by the Institutes to obtain direct access to project narrative, scientific subject, and administrative files continues to increase.

f. Training Courses

At the January STEP Module on Information Systems at the NIH, the Section, in conjunction with the Programming Unit (Systems and Data Management Section) and other NIH staff, presented a description of the CRISP system and a demonstration of its uses. In addition, an intensive instructional course and laboratory session covering the content and use of CRISP was offered on three separate occasions during the fiscal year.

g. Improvements and Other Changes in Data Processing Activities

Condensing CRISP Files. In order to improve and make more cost-effective the CRISP system, the Programming Unit of the Systems and Data Management Section condensed data contained in its files, thereby not only reducing the number of disk packs required for storage but also improving the efficiency of performing searches. The new system has been extensively tested and debugged.

CRISP History File. An additional measure to achieve increased economy in operations has involved moving all CRISP files older than 4 years from disk to tape. While this step has significantly reduced storage costs, it also has necessitated levying full charges to users for all computer expenses associated with searches against these files.

Project Narrative Files. On October 1, 1981, the Smithsonian Science Information Exchange (SSIE) went out of business, leaving CRISP and the Institutes without a machine-readable source of project narratives for research grants and intramural research projects. At the time it shut down operations, SSIE was behind on its fiscal year 1981 workload, leaving thousands of abstracts still to be processed. With the help of the initial review groups and Institutes, CRISP obtained the missing data, arranged for a contract to record the data, and subsequently incorporated the data into the CRISP narrative file. The Research Documentation Section is continuing this process for the 1982 fiscal year, and has experienced a much improved turnaround time over that provided with the former SSIE arrangement.

3. Reports, Analysis, and Presentations Section

The primary function of the Section is to satisfy the information requirements of the NIH and PHS extramural components. In fulfilling this function, the Section utilizes the IMPAC system as well as other data sources. Its responsibilities include design, maintenance, and operation of computer reporting systems; training and technical assistance in data retrieval; planning and coordination of NIH responses to annual surveys covering Federal obligations for research and development; preparation of formal publications, such as listings of NIH grants and awards and the NIH Basic Data Book; statistical analyses to compile and present visual materials dealing with extramural trends or other topics; and the development and implementation of special evaluation projects. This Section also works closely with the Systems and Data Management Section in maintaining and extending the IMPAC system, and has direct responsibility for establishing institution classifications and related computer files, as well as for ensuring the accuracy of selected key items for publications or reports.

Approximately 38,000 computer jobs were entered by the Section during the past fiscal year, primarily in response to requests for information from NIH officials, other Government agencies, and non-Government organizations. This represents a growth of nearly 15 percent over last year's total. The Section utilized all data capabilities of the NIH IMPAC system, compiled historical data, designed special reporting files, provided consultation services, and developed specifications to ensure that requesters' needs were met. In addition to hard-copy listings, the Section also supplied large numbers of magnetic tapes, which were used by requesters directly to answer questions, or which were entered into other management information systems.

a. Special Projects

During the year, a number of special projects and studies developed actual data on and projections for NIH budgets. These projects included, among others, the volume of research project applications reviewed, the number of awards and award rates, the distribution of awards by type of institution, and the average awards per

principal investigator. Reports were also prepared on estimated NIH commitments for fiscal years 1982 through 1986 in order to aid in determining future budget requirements and to ensure consistency and standard presentations of Institute projections. The Section continued to develop, test, and evaluate alternative methods for obtaining these data.

The Section continued to monitor extramural data in IMPAC, the Department of Financial Management's central accounting system, and various Institute systems to promote the credibility and efficiency of extramural reporting. The Section provided reports on obligations and commitments from the accounting system and IMPAC to the Department of Financial Management for distribution to the Institutes. For example, programs were designed to compare research and development contract and interagency agreement data in the central accounting system with those in the IMPAC system. In response to feedback from the Institutes, staff analyzed differences, and corrective actions were taken by the Institutes to alleviate problems.

In another special project, the Section studied differences between reporting concepts historically used by DRG for reporting award data and those used for preparing NIH budgets and related back-up data. Recommendations regarding policy changes to promote greater consistency will be submitted to the Office of Extramural Research and Training, NIH.

The Section developed data to show the effects of various caps on amounts awarded to determine the level of additional funds that might be generated in fiscal year 1983 for each Institute to award additional competing research project grants. This necessitated revising the current budget data for fiscal year 1983 in order to add in the 4 percent cut for noncompeting awards and the 10 percent cut for indirect costs. Reports were then prepared showing projected savings based on reductions of 1 to 11 percent in total amounts awarded.

In response to the growing concern about priority scores, staff prepared numerous reports and charts showing trends back to fiscal year 1965. Average priority scores were compiled for research project grant applications reviewed by DRG study sections for each decile, by study section, Institute, and by type of grant. Slides of some of these data were requested by the Office of Extramural Research and Training, NIH.

As a result of the continued interest in indirect costs on research grants, the Section developed data showing trends by geographic area, region, kind of institution, form of control, and Institute. These data were presented to the Director's Advisory Committee by the Director, DRG, and were also requested by the National Heart, Lung, and Blood Institute for presentation to its Council.

Proposals to limit the number of awards to an individual resulted in requests made to the Section to tabulate number of awards per principal investigator by Institute and activity. Data were developed showing principal investigators with two, three, four, or more awards, and also identifying each administering Institute and the activities supported.

The Section distributed a study of awards to departmental groups in domestic institutions of higher education. This study utilized a new computer-based system, which converts more than 4,000 department names into a smaller but comprehensive set of classifications.

To facilitate anlaysis and planning by the Office of the Director and others, the Section designed various funding models to measure the effect of budget constraints on competing awards. A sliding scale model, which can be set at any designated award rate, features a gradually declining funding rate based on priority scores.

Extensive support was given to an analysis of priority scores for competing research project grant applications. The analysis covered 15 randomly selected initial review groups and 8 fiscal years, and focused on comparisons by type of applications, size of initial review group, and high versus low budget years. The analysis was performed for both raw and normalized scores and noted the effect of normalization of scores with respect to these variables.

b. Recurring Reports and Publications

The Section continued to operate and maintain the system for reporting to Institutes currently active or fiscal year awards to date on regular monthly, quarterly, or annual schedules. The data in these reports were organized by geographic location, principal investigator, program type, grant number, budget start date, and other relevant variables. Additional reports were routinely prepared for the Institutes prior to each round of Council meetings showing detail on competing grant applications. Computer tapes were provided to a majority of Institutes on regular weekly, monthly, and annual schedules. Listings and address labels were furnished to the Division of Financial Management, Office of the Director, NIH, the Alcohol, Drug Abuse, and Mental Health Administration, the Health Resources Administration, and the Food and Drug Administration on a monthly basis, identifying grants for which reports on expenditures were overdue. The Section compiled a number of tables for each quarterly issue of the NIH Management Data Book. As in previous years, statistical summaries of initial review group actions on competing research grant and training applications were prepared during each review cycle. The NIH-Grantee Institution Interface System also provided grantee institutions with current information on awards and pending applications.

A series of tabulations of research and development contracts was provided to the Division of Contracts and Grants, Office of the Director, for inclusion in reports to the DHHS. These tabulations, which were prepared quarterly, semiannually, and annually, showed data by Institute, type of contractor, type of contract, competitive versus noncompetitive, dollar-award intervals, small businesses, minority-owned and women-owned business organizations, and other variables.

As in previous years, the Section prepared data on NIH training activities for the National Academy of Sciences. These included training awards by year, Institute, activity, discipline, specialty or field, academic level, and so forth. The Academy was also provided detailed information from each training appointment and fellowship award to update its roster of the individuals supported by NIH training programs.

The Section devoted considerable effort toward completing three annual Government-wide surveys of research and development. The National Science Foundation survey, entitled "Federal Funds for Research, Development, and other Scientific Activities," covers all NIH intramural and extramural research activities for the past fiscal year together with the estimated obligations for the next two fiscal years. The data are tabulated by performer, field of science, geographic area, basic and applied research and development, and combinations of the above. In connection with its responsibilities for preparing this survey, the Section obtained data from the Institutes to determine the amount of basic and applied research and development for each research grant and research and development contract. The second study, the annual survey by DHHS of obligations to institutions of higher education and other nonprofit organizations (known also as the CASE report), required summaries of all NIH extramural support, by activity, for individual institutions and health professional schools. Third, the Section prepared the NIH response to NIH's own annual survey of obligations for medical and health-related research covering intramural and extramural research and development obligations by scientific field, performer, program, and state.

The Section published the annual "Brown Book" series of NIH extramural awards for fiscal year 1981, including separate volumes on research grants; training, construction, cancer control, and medical library grants; and research and development contracts. The Section cooperated with the staff of the Office of the Director, NIH, in compiling data on extramural activities for the annual publication entitled Basic Data Relating to the National Institutes of Health. An analytically oriented chart book, entitled NIH Extramural Trends, Fiscal Years 1972-1981, was prepared for internal use, along with a set of slides to enable these charts and related materials to be presented effectively to various audiences. The portfolio of charts and slides was greatly expanded

this year to contain more data on priority scores and medical schools. The Section compiled quarterly reports on NIH new grants and awards and contributed to the Fogarty International Center's Statistical Reference Book of International Activities and the companion volume listing each international award.

Since May 1980, the Section's series of recurring reports has provided information on competing applications reviewed and recommended for approval, together with various statistical measures of priority score distributions, such as means, medians, standard deviations, and lowest and highest scores for each initial review group. These reports were designed to provide information enabling Institutes to evaluate and use actual priority scores for decisions formerly based on normalized priority scores.

In order to further help the Institutes that formerly relied on normalized priority scores, the Section, in cooperation with the National Heart, Lung, and Blood Institute, has operated a system for ranking grant applications on a comparable basis, using percentile distributions of actual (raw) priority scores. These distributions are stored in the IMPAC system for all competing applications to facilitate preparing paylists and other reports to Councils. A variety of computer-generated charts were regularly distributed to the Institutes and DRG administrative staff to facilitate comparisons of priority scores and recommendation rates for the various DRG study sections.

The Section also served as the authoritative source for information on the workload of DRG study sections. Several weeks after the cutoff dates for receipt of applications for review cycles, statistical tabulations were prepared showing the volume of applications to be reviewed by each study section and Council, the type of application, the primary and possible secondary potential awarding Institutes, and the requested budgets. Following the completion of each review cycle, special summaries of DRG study section actions were provided to assist in managing and monitoring their activities.

The Section worked closely with staff in the Office of the Director, NIH, in developing and preparing reports on NRSA fellowships and other trainees. These reports present the data along two axes: one, scientific discipline, is a group of new lexicon DSF codes; the other, program area, is a grouping of codes unique to each of the Institutes.

c. Systems Support and Development

The Section maintained the IPF, which is the central registry of names, locations, and other selected information for organizations participating in PHS extramural programs. This file assured uniform reporting and eliminated the necessity for storing similar

information in individual grant and award files. Approximately 400 new records were added to the IPF, along with more than 25,000 item updates. The IPF now contains about 27,000 records. In order to use personnel and computer resources more effectively, the Section modified maintenance procedures to cover only organizations that applied for grants or received contracts since fiscal year 1971. This change reduced the workload by about 50 percent, without significantly affecting the accuracy of reports.

The PHS Grants Data System was supplied monthly magnetic tapes of all grant records contained in the IMPAC system and the IPF codes for institutions newly recorded in the Grants Data System. This support facilitates consistent and accurate PHS-wide reporting.

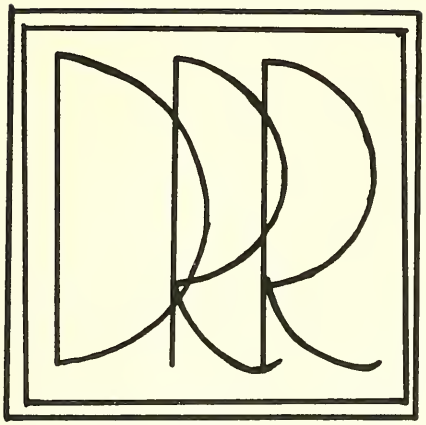
The Section continued to develop and maintain the index of major components and departments for institutions of higher education. This index and related computer program edits ensured consistent coding of applications and awards for medical schools and others. During fiscal year 1982, approximately 200 new department codes were added to the index, along with more than 7,500 item updates. The index now contains information on about 2,200 institutions of higher education, approximately 16,600 major components and departments, and about 3,000 reference lines for internal use. As in previous years, this Section was responsible for creating and maintaining a special set of fiscal year publication files, which serve as authoritative sources of data to determine trends or year-to-year changes in the amounts and distribution of NIH extramural awards. A special subset of these files was established to contain data needed for NIH reports on basic and applied research and development. In preparing these data, the Section interacted extensively with the Office of Program Planning and Evaluation, Office of the Director.

In response to the large number of requests for reports that compare or rank institutions by such factors as dollars awarded or other success-related statistics, the Section has greatly expanded its capacity to provide such statistics in a consistent and usable manner. Included is a standardized procedure for providing each institution with a table showing 12 year trends and rankings for numbers of competing research project applications, approval or success rates, and priority scores. Trend data are available based on either the number of applications or the dollars requested. In addition, corresponding NIH profiles are available, which permit comparison of such statistics as the NIH average with high, low and median institution statistics.

Work continued with a contractor to add data from NIH Research Grant Expenditure Reports for the 1976 to 1978 fiscal years to the existing file for fiscal years 1971 to 1975.

d. Retrieval Training

The Section has long been responsible for assisting Institutes in developing and applying systems and programming techniques that would facilitate independent use of the IMPAC system. A senior computer specialist provided these services on a full-time basis. During the year, basic courses were offered on how to use the Inquiry and Reporting System.



DIVISION OF RESEARCH RESOURCES

ANNUAL REPORT

FISCAL YEAR 1982

(October 1, 1981 - September 30, 1982)

National Institutes of Health
Bethesda, Md. 20205

MISSION:

Identifies and meets the research resources needs and opportunities of the NIH by conceiving, creating, developing, and assuring the availability of those resources that are essential for the efficient and effective conduct of human health research.

Helps institutions establish and operate general clinical research centers where research studies can be conducted on patients over a wide range of human diseases; supports highly sophisticated biotechnology resources, such as computer centers, high voltage electron microscopy centers, and biological structure determination centers; supports primate research centers; increases and improves laboratory animal facilities and resources; makes awards for minority biomedical support, and provides institutional research support for stabilizing and developmental efforts among a variety of institutions throughout the United States.

Provides a unified approach to solving the many complex needs of health-oriented research that tends to be institutional, regional, or national in scale.

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REPORT OF THE DIRECTOR

Dr. James F. O'Donnell
Acting Director
Division of Research Resources

I. Report of the Acting Director

The Division of Research Resources (DRR) continued to operate during Fiscal Year (FY) 1982 with an Acting Director while the Search Committee worked toward the identification of a slate of highly-qualified candidates. On September 15, 1982, the Director of the National Institutes of Health (NIH) announced the appointment of Dr. Betty H. Pickett, to be effective October 1, 1982.

Despite the fact that the Division was without permanent leadership for 21 months, and in light of the budgetary constraints facing all NIH activities, the organization and its Programs continued to prosper. Significant new Program activities included the initiation of the Shared Instrumentation Grant Program, funding several new Biotechnology Resources, joint funding by the General Clinical Research Centers Program and the Minority Biomedical Research Support Program of a small General Clinical Research Center at Meharry Medical College, and joint funding by the Animal Resources Program and the Minority Biomedical Research Support Program of two new animal resource improvement grants at minority institutions.

The Division also initiated a new activity, Biomedical Research Models. The purpose of the activity is to examine the extent of use of lower organisms and nonliving models in NIH-supported research and to explore the scientific potential for the development of additional models.

The development of models is often an essential step in the process of understanding complex biological phenomena. Research activities employing simpler systems as models (lower organisms or tissues and cells in culture) often seek to answer questions of biological processes common to all living things. Available simpler model systems may provide data which would be expensive, difficult, or impossible to obtain using higher animals as research subjects. In times of increasing restraints on research budgets, it seems advisable to determine if any of these specific simpler systems have general applicability. Intensive interest focuses on such developments today because of their potential for accelerating research findings, of dealing with multiple variables, of responding to public concerns (animal welfare), and of reducing the current costs of biomedical research. The tremendous range of biomedical research activities involving models which differ phylogenetically, structurally, and conceptually can be appreciated from an inventory of the NIH grants program. Research efforts employing model systems other than higher animals can be identified in the grant portfolios of several Institutes; indeed, this is an activity of trans-NIH interest and importance.

An inventory has been made of research models employed in Public Health Service (PHS)-supported research projects, and an interest and need for new biomedical research models have been identified through contact with officials of other agencies (Food and Drug Administration, National Academy of Sciences, National Science Foundation, and Department of Education). Study of the results of the PHS inventory allows identification of research models employing lower organisms, tissues/cells in culture, or nonliving systems; pools of individual investigators having established expertise in each of

the areas of potential model development; and potential model development areas currently supported by several NIH Institutes.

The results of this survey have been placed on the WYLBUR computer system at NIH; this permits specific keyword searches to be employed in developing an information clearinghouse and in identifying specific Workshop participants. Workshops are planned for 1982/1983 to: (1) identify areas of research which might benefit from the development of new or improved models for biomedical research; (2) determine the characteristics and essential elements of current research models which promote their interdisciplinary applicability; (3) examine specific ongoing modeling activities for the potential general applicability; and (4) suggest mechanisms for promoting the development of models deemed meritorious and necessary.

In FY 1981, the Division began a comprehensive, systematic effort intended to produce Program performance data on all the Division's major Programs and major subprograms for use in Program management and planning activities. This activity is being carried out in four phases:

Agreed-Upon Objectives and Indicators (Phase One): During the period March through November 1981, the objectives of all DRR Programs and the major subprograms were set out in as measurable terms as possible. Indicators were developed for the objectives, and the finished products became the basis for, and an integral part of, the summaries being prepared in Phase Two.

Program Performance Summaries (Phase Two): From November 1981 through September 1982, Program performance summaries were developed for the Programs, using the Phase One agreed-upon objectives and indicators and requiring that all parts of the Program performance summaries were written in terms of the agreed-upon objectives and indicators. The completed summaries were distributed to the various evaluation offices in the Office of the Director, NIH, PHS, and the Office of the Secretary, Department of Health and Human Services.

Short-Term Evaluations (Phase Three): Building on the summaries, short-term evaluations of the Division's Programs are being performed. The short-term evaluation of the Minority Biomedical Research Support Program commenced on August 30, 1982, and the evaluation of the Biomedical Research Support Program is projected to begin about January 1983. The evaluations of the other Programs are expected to follow at three- to five-month intervals. The Phase Three study results will be distributed throughout the Department and will be incorporated into the Division's Five-Year planning process.

Evaluation Decision-Making for FY 1984 and Beyond (Phase Four): Taking into account the Program performance information available in the summaries and resulting from the short-term evaluation of each Program, DRR management will decide on the need for, as well as the desirability and timing of, further evaluation of the Division's Programs. This process will be facilitated by the methodology for further evaluation developed for each Program as part of its short-term evaluation during Phase Three.

The DRR peer review activities are located administratively within the Office of the Director. Although each of the Division's five Programs awards grants which require initial review, only applications to the Animal Resources Program, the General Clinical Research Centers Program, and the Minority Biomedical Research Support Program are reviewed by Committees managed by DRR. Applications to the Shared Instrumentation Grant Program of the Biomedical Research Support Program and to the Biotechnology Resources Program have been reviewed within the Division of Research Grants.

During FY 1982, the DRR staff conducted initial review of 147 grant applications including 67 project site visits. A full range of review procedures and mechanisms was used, some of which were developed within DRR. This included project site visits, panel reviews, and review by conference calls.

Historically, Biotechnology Resources' grant applications have been reviewed by the Division of Research Grants. Several different mechanisms of review have been utilized in the past, and we are currently examining them and exploring other alternatives. Our objective is to assure the most equitable review of these applications which have widely disparate technological and disciplinary foci. Our interest in examining this review process is shared by members of the Biotechnology community, and we are considering the suggestions for improvement they have offered.

Review of activities related to the PROPHET Computer System is done by the Biotechnology Resources Review Committee. During FY 1982, four prospectuses for new PROPHET sites were reviewed. In addition, three ongoing sites were also reviewed. One contract proposal involving the CLINFO System was evaluated by an ad hoc panel.

Applications to the Shared Instrumentation Grant Program, a new initiative of the Biomedical Research Support Program, were reviewed by the Division of Research Grants using a process already established for another NIH program. A total of 203 applications was reviewed using primarily ad hoc committees.

The Division continued to respond to the information needs and concerns of its biomedical research constituency and of the lay public through its Office of Science and Health Reports (OSHR) and its Research Resources Information Center (RRIC). The Center was established under contract by OSHR in 1976 to promote greater understanding of the role played in NIH-sponsored biomedical research by the Division's research resources.

Under the technical guidance of the DRR Information Officer, the services and products of the Center continued to expand. The circulation of the Research Resources Reporter topped 22,000, with newsstand distribution from 16 newsstands located throughout the NIH campus around 6,000. Two awards for editorial excellence were presented to the Division's RRIC publications during the year.

The 1981 DRR Program Highlights, a compendium of Division information for the year, was written by the RRIC. Among other publications, the Center produced the revised Animal Resources Directory (4th Edition) and the

Minority Biomedical Research Support Directory (5th Edition); the General Clinical Research Centers Directory was in the early stages of revision.

The OSHR was involved in numerous other communications projects during the year. Special events were highlighted through a number of activities. Early in the year, the Office arranged coverage of the dedication of a new animal research building at the New England Regional Primate Research Center. A story and photo feature on the Center were carried on the Associated Press national wire, appearing in over 107 newspapers.

Also early in the Fiscal Year, the Newspaper Enterprise Association carried a Division-written feature on infant vision which credited the Biomedical Research Support Grant (BRSG) for support. In connection with the BRSG, the Office also worked with the authors of "When Research Needs Rescue," published in the November/December 1981 issue of AGB Reports from the Association of Governing Boards of Universities and Colleges. They highlighted the importance of the BRSG to the academic community.

Mid-November saw the celebration of the twentieth anniversary of the DRR Primate Research Centers Program at the Yerkes Regional Primate Research Center. This event featured a press briefing conducted by the Office.

A twentieth anniversary program for the General Clinical Research Center (GCRC) at New York University (NYU) Medical Center included press activities arranged for by OSHR. Numerous releases on research in the GCRC emanated from NYU following the celebration.

An OSHR-initiated media briefing took place in January at the Medical College of Wisconsin. The story dealt with the relationship between the location of body fat and the subsequent development of diabetes in women. Media interest in this event was intense.

In April, the Minority Biomedical Research Support (MBRS) Program held its Tenth Annual Symposium. The past year's Symposium was coordinated by the University of New Mexico and was held in Albuquerque. The OSHR operated a press room for the largest gathering of minority scientists in the United States. Numerous local radio and television programs carried Program personnel as guests. In addition, interviews were prepared and fed throughout the Symposium to the National Black Network in New York and the Sheridan Black Network in Alexandria, Virginia.

In mid-July, an investigator at the University of Cincinnati General Clinical Research Center reported to the media on the results of clinical trials of a new cooking fat substitute called "sucrose polyester." The briefing, organized by OSHR, was extensively covered by many media representatives.

Several modular exhibits with information on the national General Clinical Research Centers Program were furnished to Clinical Research Centers in different sections of the United States. Displays were arranged with Harbor-UCLA Medical Center GCRC, Torrance, California; the University of Michigan GCRC, Ann Arbor; and the University of Alabama GCRC, Birmingham.

The OSHR also conceived and produced two full-sized exhibits on the Division during the year. The first exhibit was built for permanent display in the Ambulatory Care Research Facility, NIH, and the second was constructed to be sent to various meetings throughout the United States. It was first shown and staffed by Office personnel at the Ninth Congress of the International Primatological Society in Atlanta, Georgia.

In addition to its communications' activities, the Office received and processed approximately 25 Freedom of Information requests. Approximately 88 hours of clerical and professional time were spent in handling these requests. The Office also handled 150 Privacy Act requests which, for the most part, were for copies of summary statements of grants before the National Advisory Research Resources Council meeting. These requests took approximately 150 hours of clerical and professional time.

The mission of the Office of Administrative Management (OAM) of the Division is to provide administrative support services to the Division's staff which are necessary to fulfill the scientific mission of the Division. In 1982, the OAM staff efforts focused on enhancing the availability and flow of information for Program planning and analysis purposes, on providing accurate and reliable financial and personnel management information, and on handling all administrative needs for optimal functioning by Division staff.

Three primary computer systems were the main focus of the Data Management Section:

DRR Information System: To facilitate easier use by the DRR staff, most of the User's Guides were revised, reformatted, and reissued. The Minority Biomedical Research Support system was enhanced to include annual report data. In addition, most of the Program-specific subsystems were revised to reflect changes in data collected from annual reports.

Scientific Subproject System: The latest complete fiscal year data were collected into files for scientific searching by the DRR Special Projects Staff. This was processed by two systems running concurrently. It is expected that future years' data will be processed under the new system which is in its final stages of testing.

User Data System: The staff has devoted considerable time and effort in designing and programming this system. One outstanding accomplishment was computerizing the process of matching the names of the users of DRR resources, thus speeding up the availability of the data by as much as six to nine months. In addition, many reports were revised or enhanced for clarity and consistency. Many new reports were added. Additional summary tables, as well as graphics, are now being programmmed.

Within the Financial Management Section, the staff assumed full responsibility for, and carried out all aspects of, the execution, formulation, and presentation of the Division's budget. In light of severe budgetary constraints, more innovative and effective budgetary and financial management strategies were planned and implemented. As a result, the

Division received the second highest percentage increase of all the major NIH Institutes in the 1983 President's Budget request.

The Personnel Management staff assisted in the search for a Director for the Division. In addition, they successfully implemented the new Employee Performance Management System (EPMS), including providing training and information sessions for both supervisors and employees. Also, the Merit Pay performance standards were revised and implemented to include three levels for each element. In their daily operations, the Personnel Management staff complied with the DRR Affirmative Action Plan and the Federal Equal Opportunity Recruitment Program, while continually informing the DRR personnel of new or changing personnel policies and procedures.

Within the Administrative Operations Section, the daily administrative needs of the Program staff were handled quickly and competently. All procurement actions, travel orders, maintenance and repair orders, space changes, and other miscellaneous functions were performed by the Administrative Operations staff. The NIH Delegated Procurement (DELPRO) System was implemented in the Division in 1982 to expedite the procurement of certain supplies and services for the Division.

For many years the Division has had an Equal Employment Opportunity (EEO) Committee, composed of representatives from various ethnic groups, different grade levels, and organizational components. The DRR Personnel Officer, the DRR representative to the NIH Women's Advisory Committee, and the DRR-EEO Counselor are ex-officio members. The DRR does not have an EEO Coordinator or Officer.

As part of a continuing effort to have an active and productive Affirmative Action Program, the Division's Committee spent a number of months this past year in designing and producing an employee training booklet. Covered in the booklet are the DRR Program descriptions, different kinds of training opportunities in general, and related career opportunities and work experiences. Not only of value to current employees, the booklet will also be useful in orienting new employees. Distribution to all DRR employees will occur late this year.

As in past years, the Committee supported a broad array of lunchtime programs with guest speakers. This medium of information exchange, while it chiefly contributes to heighten employee awareness on selected topics, further benefits the DRR by increasing the degree of group interaction between employees.

One EEO Committee meeting this year concentrated on helping members gain a more in-depth understanding of the affirmative action policies, problems, and practices within the NIH, the Department, and in relation to the Division. The Acting Director, Division of Equal Opportunity, NIH, who the Committee invited to lead the discussion, gave both old and new members a lively and detailed resume of past issues and events and future outlooks. His comments and views were particularly useful in clarifying ways that the DRR Committee could participate with the activities focused in his office.

During the year, the Division also established a small task force to develop its Affirmative Action Plan for 1982. That effort was productive in identifying some potential new areas for activities with more realistic action items and milestones.

As the new Fiscal Year of 1983 begins, the Division of Research Resources looks forward to effective pursuit, under its new leadership, of its critical contributions to biomedical research.

Animal Resources Program

INTRODUCTION

The overall objective of the Animal Resources Program is to support resource projects that provide, or enable scientists to use effectively, animals in human health-related research. Special attention is given to those animal resource activities that are broadly supportive of the missions of the various NIH components. The objectives are accomplished through the Primate Research Centers Program and the Laboratory Animal Sciences Program.

PRIMATE RESEARCH CENTERS PROGRAM

The Regional Primate Research Centers Program was initiated by NIH during the period 1961-1965. The original objective was to meet a recognized need for suitable facilities and appropriate research environments where biomedical research employing the nonhuman primate could be best conducted. Seven Regional Primate Research Centers (RPRCs) were constructed, equipped, staffed, and became operational as unique research institutions by 1965. These Centers and their respective locations are: University of Washington RPRC, Seattle, Washington; Oregon RPRC, Beaverton, Oregon; California RPRC, Davis, California; Delta RPRC, Covington, Louisiana; Yerkes RPRC, Atlanta, Georgia; New England RPRC, Southborough, Massachusetts; and Wisconsin RPRC, Madison, Wisconsin. Each Center is affiliated with a host academic institution. The Centers have resources and research environments which are suitable for a broad range of biomedical research. The Animal Resources Program provides core operational support for the Centers through resource grants. Research projects at the Centers are funded largely by NIH categorical Institutes, other Federal agencies, and private foundations, through grants and contracts which are held by core staff and collaborative and/or affiliated scientists. Through their use of nonhuman primate models, these scientists have made numerous important contributions to biomedical research. During the past year, significant investigations have been carried out in various biomedical areas, including reproductive biology, infectious diseases, behavioral sciences, neurosciences, toxicology, nutritional and metabolic diseases, and environmental health.

Core support in the amount of $18.373 million provided by this Program in fiscal year 1982 enabled the 143 core staff, doctoral-level scientists to conduct research in the Centers. In addition, the resources and services of the Center were made available to 507 affiliated, collaborative, and visiting scientists from various academic institutions. Research training environments were provided for 188 graduate students engaged in thesis-related research. The Program provided salary support for 680 doctoral-level, technical, and administrative staff personnel.

On a regional basis, the Centers provided a total of 5,080 biological specimens to 333 scientists at various research institutions throughout the United States. Scientific productivity within the seven Centers has remained strong during the past year, with 550 journal articles, books and book chapters published by the core staff and affiliated/collaborative scientists.

Because of the problems associated with obtaining certain species of nonhuman primates from countries of origin, all seven Centers have continued their domestic breeding efforts. Approximately 2,100 live births, embryos and fetuses were produced by the seven Centers in 1981, representing nearly 75 percent of their total primate animal requirements. Nuclear colonies of a number of less commonly used primate species have also been maintaind to assure the survival of these species for potential research needs in the future. A total of approximately 13,000 primate animals representing 44 species were maintained by the Centers in 1981 for research and domestic breeding uses.

Major research emphasis areas and selected examples of research activities at each Center during the past year are as follows:

CALIFORNIA REGIONAL PRIMATE RESEARCH CENTER, UNIVERSITY OF CALIFORNIA AT DAVIS

The major research areas at the California Primate Research Center relate to environmental health sciences, infectious diseases, perinatal biology, behavioral biology, respiratory physiology and immunology. An example of activities at the Center during 1981 is as follows:

Comparative Teratogenicity and Pharmacokinetics of Corticosteroids

As part of their continuing interest in the effects of potentially teratogenic drugs and environmental agents on the developing fetus, Center investigators have investigated the teratogenicity and pharmacokinetics of several commonly used corticosteroids. Studies on the teratogenicity of high doses of triamcinolone acetonide (TAC) in the rhesus monkey have been previously described. In order to evaluate dose-response characteristics of TAC embryotoxicity, pregnant rhesus monkeys were treated with TAC at two lower doses. Defects, grossly similar to those found previously occurred in all cases treated with 2.5 mg/kg/day throughout organogenesis. A markedly decreased incidence and severity of defects was elicited after a dose of 0.5 mg/kg/day.

Preliminary studies with dexamethasone (DEX) indicated that a dose of 1 mg/kg did not induce any gross malformations when given on alternate days between days 23 - 31, but induced mild defects in fetuses treated throughout organogenesis. The effects of higher dose rates are currently being evaluated. This data will allow comparisons of the teratogenic potency and dose-response characteristics of TAC and DEX.

A high performance liquid chromatography technique has been developed for the separation of radiolabeled corticosteroids and their metabolites in plasma, urine and tissues from pregnant rhesus monkeys. This methodology has been used in pharmacokinetic studies of TAC and Cortisol (C). The initial results indicated that following the simultaneous maternal administration of TAC and C to pregnant rhesus monkeys during late gestation (day 130), a greater % of TAC than C was distributed in the plasma and tissues of the fetus. These studies have now been extended to investigate the influence of dose on the transplacental pharmacokinetics of TAC while holding the dose of C constant.

The results demonstrate that neither the dose of TAC (over a 5,000 fold range) nor route of administration (im vs. iv) appear to modify the observation that after maternal administration of TAC and C, a larger % of TAC than C is distributed in the fetus.

Experiments are currently underway to test the hypothesis that TAC, by virtue of its greater fetal exposure, poses a greater teratogenic risk than C when given at equivalent therapeutic doses.

The results of these studies will be important for the assessment of potential teratogenic or toxic effects on developing embryos of women who are administered these types of anti-inflammatory agents, particularly during critical stages of pregnancy. Pregnant rhesus monkeys are excellent animal models for these prenatal studies.

DELTA REGIONAL PRIMATE RESEARCH CENTER, TULANE UNIVERSITY

The Delta Primate Research Center core research programs cover the areas of microbiology and infectious diseases, immunology, parasitology, biochemistry, neurobiology and urology. The affiliate/collaborative program includes a number of other areas, including vision research. An example of their research projects is as follows:

Neurobiological Studies Related To Motion Sickness

A new technique was developed which makes it possible to localize functional brain areas of the squirrel monkey which are associated with the emetic response (vomiting) of motion sickness. This method involves the use of sequential double isotopically labeled 2-deoxyglucose (2-DG) and permits identification of brain sites or functional cell groups which mediate specific physiological functions. Following injections of the two isotope-labeled compounds the (^{3}H) and (^{14}C) 2-DG become metabolically "trapped" in the activated sites. The animal is then restrained in a chair with the head tilted forward about 20 degrees. The chair is attached to a rotating platform on the motion testing machine, and one of the two animals in each experimental chair is then subjected to a "standard" motion regimen for 45 minutes. The second animal in each experimental pair is maintained in a quiescent stage for the same length of time.

After sacrifice, the medulla oblongata, cerebellum and cervical spinal cord of each animal are dissected, frozen in liquid nitrogen and cryostat sections are cut. The radioactivity of the (^{3}C) and (^{14}C) labeled 2-DG in the samples are determined by liquid scintillation counting. Ratio comparisons of the concentrations of (^{3}H) 2-DG to (^{14}C) 2-DG in the different brain structures of motion-activated animal and quiescent animal are made to determine those sites which mediate the vomiting response to motion sickness.

This new research method will greatly facilitate basic neurological studies which seek a greater understanding of motion sickness and improved methods for its prevention and/or treatment. The method will also be useful in other human health-related studies involving the effects of various stimuli on neural pathways. One potential application will be in studies designed to

determine if metabolic changes occur in the vestibular portions of the brain with age.

NEW ENGLAND REGIONAL PRIMATE RESEARCH CENTER, HARVARD UNIVERSITY

The New England Primate Research Center's core research program covers the areas of microbiology and infectious diseases, psychobiology, comparative pathology, viral oncology, cardiovascular physiology and nutrition. The Center's extensive affiliate and collaborative research programs include numerous other biomedical areas of investigation. An example of research activities at the Center during the past year is as follows:

Experimental Myopia In Primates

Axial myopia (nearsightedness) is a significant optical defect which affects millions of people. This condition causes the image to be focused in front of the retina because the axis of the eyeball is too long. The major objectives of this project are to investigate the mechanisms responsible for the genesis of axial myopia and to develop procedures to treat and/or prevent the condition. Three species of macaques (Macaca mulatta, Macaca arctoides and Macaca fasicularis) are being used as animal models for the studies, since neonatal eyelid closure or corneal opacifications produce marked axial myopia and characteristic fundus changes in these species.

The central nervous system plays an important role in the development of myopia. Therefore, the effects of interrupting afferent and efferent pathways on the lid-closure myopia are being investigated by intracranial section of the optic nerve, the trigeminal nerve and the occulomotor nerves. Previous work has indicated that atropine administration will prevent axial myopia in M. arctoides, but not in M. mulatta. The role of accomodation is being studied further by: 1) removal of the ciliary ganglion, 2) electrical stimulation of the ciliary ganglion, and 3) by forced accomodation through behavioral methods. Induction of myopia through distortion of the visual input without eyelid closure or corneal opacification is also being attempted by raising the monkeys with translucent occluders of known light transmitters and by using positive lenses which prevent distinct vision without attentuating light. The results of these studies on nonhuman primates should lead to an improved understanding of the causes, as well as possible methods of prevention or treatment of this human optical defect.

OREGON REGIONAL PRIMATE RESEARCH CENTER, OREGON HEALTH SCIENCES UNIVERSITY

Major areas of research emphasis at the Oregon Primate Research Center include reproductive biology, perinatal physiology, cutaneous biology, immunology, nutrition, toxicology, and metabolic diseases and behavior. An example of activities during the past year is as follows:

Gossypol Inhibition of Sperm Energetics and Mobility

Gossypol has been reported in the Chinese literature to be an effective oral male contraceptive agent. The mechanism of action unknown, although the compound has been shown to inhibit sperm respiration, glycolysis and motility

in vitro. The latter results led to a hypothesis that this compound may have potential as a topical vaginal contraceptive. To circumvent the inherent shortcomings of detailed chemical studies on human semen (variability in semen samples and lack of sufficient material obtained under carefully controlled conditions), a study was performed with semen obtained from rhesus macaques (Macaca mulatta). Gossypol was found to be a potent inhibitor of monkey sperm glycolysis and motility when respiration is blocked by an electron transport chain inhibitor. Significantly, the inhibition of both processes depends not on the absolute concentration of gossypol, but rather on the gossypol:sperm ratio. At a ratio that inhibits glycolysis by approximately 50%, Center scientists determined the enzymatic sites at which gossypol acts on the glycolytic sequence and showed that gossypol affects enzymes requiring adenosine triphosphate (ATP) as a substrate or an allosteric effector. It was also shown that all adenine nucleotides, including ATP, adenosine diphosphate (ADP) and adenosine monophosphate (AMP), are markedly reduced with increasing levels of gossypol. These results indicate that gossypol acts primarily on enzymes involved in nucleotide metabolism to inhibit sperm viability, rather than on specific enzymes of the glycolytic sequence.

This study will provide basic information concerning the mechanisms of action of gossypol and should provide valuable insights into its potential anti-fertility effectiveness and safety as a human contraceptive. Additional studies of this nature will undoubtedly be necessary before favorable consideration can be given to initiating human clinical trials in the United States.

WASHINGTON REGIONAL PRIMATE RESEARCH CENTER, UNIVERSITY OF WASHINGTON AT SEATTLE

The core research program of the Washington Primate Research Center includes the areas of neurological sciences, cardiovascular function, developmental biology, disease models, endocrinology and metabolism, and craniofacial structure and function. An extensive affiliated scientist program involved over 60 investigators who were engaged in a variety of investigative areas. An example of research activities during the past year is as follows:

Hemispheric Lateralization of Speech Perception

The study of hemispheric lateralization of speech perception, although traditionally limited to research on humans, is one of the most active areas of inquiry in the biology of language. Psychophysical investigations of neural lateralization of phonemes, the smallest units of speech, have recently demonstrated a basic division between vowels and consonants which, in some individuals, is related to the phenomenon of hemispheric lateralization of function. The fact that not all subjects display this neural division of phonetic units suggests that individual differences in hemispheric lateralization of speech perception, almost totally neglected in laterality research thus far, are a fundamental aspect of the phenomenon. To demonstrate hemispheric lateralization of speech perception in nonhuman primates, baboons (Papio cynocephalus) were studied for lateralization of synthetic vowels (a, i) and consonants (b, p) in a monaural auditory

discrimination task with food as reward. All animals showed highly significant and reproducible ear advantages for vowels and consonants, but not for pure tones. Two of the subjects showed a clear dissociation of vowels and consonants in opposite directions between the cerebral hemispheres. The other two exhibited a distinct left-ear advantage (right-hemisphere dominance) for both vowels and consonants. The data also suggest that neither age nor sex interacts significantly with either the pattern or the degree of ear asymmetry. The results are in fundamental agreement with recent human findings, and represent the first evidence of hemispheric lateralization of speech perception in a nonhuman species. This could also provide valuable information on the evolution of speech and language.

WISCONSIN REGIONAL PRIMATE RESEARCH CENTER, UNIVERSITY OF WISCONSIN AT MADISON

Focused areas of research at the Wisconsin Primate Research Center include endocrinology, behavior, neuroscience, reproduction and pathology of environmental pollutants. An example of research performed during the past year is as follows:

Advances in In Vitro Fertilization

Rhesus monkey (Macaca mulatta) and golden hamster spermatozoa and eggs were used by Center scientists to study fertilization and embryo development in a culture medium. Rhesus sperm were not able to fertilize eggs unless they were first incubated with cyclic nucleotide stimulators (caffeine and dibutyryl cyclic AMP). In addition, incubation of sperm with these stimulators caused development of a "whiplash" form of motility (hyperactivation) that has not previously been described in sperm of higher primates, but which is well known to be correlated with acquisition of fertilizing ability by rodent spermatozoa. Evidence of sperm penetration was obtained using in vitro matured rhesus eggs, the first time this has been observed. A few of these eggs cleaved to the 2-6 cell stage, but most were defective. In a series of experiments with in vivo matured eggs, 58% showed evidence of fertilization, including 11 eggs that cleaved to 8-16 cell stages. The timing of embryo development in vitro was comparable to that reported for in vivo development of rhesus monkey embryos. The effects of catecholamines in stimulating sperm fertilizing ability was further examined with a hamster in vitro system. Sperm were able to fertilize eggs when addition of epinephrine was delayed just as well as when epinephrine was present throughout sperm incubation. This finding suggests that the requirement for catecholamines does not develop until sperm are well into the process of capacitation. Investigations on these model systems are important for the achievement of a more complete understanding of the basic processes associated with in vitro fertilization and possible future application of this technique to humans.

YERKES REGIONAL PRIMATE RESEARCH CENTER, EMORY UNIVERSITY

Research at the Yerkes Primate Research Center includes psychobiology of great apes and monkeys, anatomical and physiological aspects of the central nervous system, pathology, reproductive biology, immunology, language

acquisition and development of primate models of human diseases. An example of their activities during the past year is as follows:

A Potential Primate Model For Human Cystic Fibrosis

Investigations have continued on the development of a naturally-occurring animal model for cystic fibrosis (CF), which is desperately needed for studies on this disease. Evaluations are being made on the possible genetic transmission of a cystic fibrosis-like pancreatic disease which occurred spontaneously in a young rhesus monkey. This animal died at the age of six months of unknown causes at the Yerkes Center. No other cases of this nature have previously been reported in the scientific literature. The current project is basically an eight-year breeding and testing program utilizing the parents, grandparents and aunts of the index case in an attempt to determine if the observed pancreatic disorder can be genetically transmitted. The establishment of a rhesus monkey breeding colony with this genetic trait, and subsequent production of animals with the CF genetics trait, would be a great asset to research on this disease. A line breeding program has been established and 31 offspring have been produced during the first two years of this project. Sixteen female offspring are currently available for production of the F_2 generation. Screening tests for exocrine pancreatic function (fecal trypsin, serum isoamylase) and the pilocarpine ionophoresis sweat tests are being conducted (as indicators of the CF pancreatic disease) on the offspring of the breeding program and have yielded essentially normal results to date. If these long-term studies are successful, an invaluable animal model system will be available to investigators for studies on human cystic fibrosis.

LABORATORY ANIMAL SCIENCES PROGRAM

The Laboratory Animal Sciences Program (LASP) assists institutions in developing and improving animal resources for biomedical research and training through the award of research and resource grants and contracts. Program areas include support for research related to important laboratory animal disease problems, animal colonies which serve as national resources for biomedical research, studies directed at finding animal models which are needed for research on human diseases, projects to assist institutions to comply with the legal and policy requirements for care of laboratory animals, laboratories for the diagnosis and control of diseases of laboratory animals, and research training of specialists in the field of laboratory animal medicine. The Program awarded funds totaling $7,810.5 million in fiscal year 1982, which supported 62 grants and 5 contracts relevant to animal research or resource activities, 10 institutional training programs, and two individual fellowship awards.

RESOURCE RELATED RESEARCH

The majority of projects falling into this category involve investigation of the etiology, pathogenesis, and control of laboratory animal disease problems. For example, currently active projects include the diagnosis and control of mammalian encephalitozoonosis, experimentally induced mucoid enteritis in rabbits, and control of respiratory mycoplasmosis in rodents. The encephalitozoonosis project has resulted in the development of a simple, rapid test for detection of serum antibodies in rabbits. The disease is

frequent (about 20% of all rabbits) and ubiquitous, thus demonstrating the potential for complicating research. Ongoing studies are evaluating chemoprophylaxis and continuing to clarify the pathogenesis of the disease and the immunologic impact of infection on the host.

In addition to disease related studies, two ongoing projects are focused on population studies of nonhuman primates in countries of origin. These include census studies of rhesus monkeys in northern India and important habitat features relative to West African rain forest primates. The former (India) project was begun in 1959 (supported by ARB since 1973) and has provided data regarding population dynamics, demographic, and reproductive parameters of a natural rhesus population. One study group has increased in numbers 16.8% in the last 4 years since the export ban on rhesus monkeys compared with an increase of 16.5% in the 4 years prior to the ban. Since populations with good birth rates and low infant mortality rates can increase at the rate of 16% per year, the rhesus population could have been expected to increase at least 50% since the ban. The actual figures indicate that similar factors influenced the population before and after the ban and that export *per se* has not been a dominant factor. Ongoing studies will provide data on the effects of habitat displacement which is occurring with one study group and the feasibility of intentional transplants and relocation of breeding groups. Such information is necessary as a guide to conservation and management of rhesus monkeys and will be important in evaluating the potential supply of rhesus monkeys for biomedical research.

A relatively new project (initiated in 1979) involves genetic investigations in rhesus monkeys at the Wisconsin Regional Primate Research Center. In particular, additional genetic markers are being sought in order to develop a multiple locus measure of inbreeding. To date, 1,825 monkeys have been typed for 16 blood group systems and 3 isozymes and 5,404 animals are on file that have been typed for standard genetic markers. Three new blood group systems, each with two alleles have been discovered. Twenty-eight inbred animals were discovered in the data set. A higher infant mortality rate (18% versus 12.5% for the rest of the colony) was noted in this group as might be anticipated from the known effects of inbreeding. The feasibility of introducing new genes into a closed troop through adoption of newborn infants (interchange of newborn animals within 3 days with outside mothers and outside orphan infants) appeared feasible in preliminary studies. Information from this project will be particularly important in developing various genetic management strategies relative to culling and breeding in domestic breeding colonies at a time when the availability of new animals is very limited.

The number of resource related projects has been relatively level in recent years (9-12 active projects). There is a growing recognition that naturally occurring laboratory animal diseases and environmental factors can have a significant effect on research projects. This year one new project was awarded which is aimed at developing a live vaccine against rabbit pasteurellosis. This is an extremely important area since pasteurellosis is the primary cause of death in weanling and young adult

rabbits and a common complication in experimental situations where it is often latent or subclinical.

ANIMAL MODELS AND SPECIAL COLONIES

The major objectives of this program area are: (1) to define, characterize, and exploit the relevant biological attributes of selected animals which display potential for use in biomedical research and (2) to establish, improve or expand special colonies of well-characterized animals which are of proven value for biomedical research, but which are not generally available from other sources.

Projects aimed at the first objective are of two general types. The first is represented by an active resource at Washington State University which involves a multidisciplinary effort to identify, characterize, and make available new animal models of human genetic diseases. Input regarding potential models is sought from a variety of sources, including animal clinics, veterinary practitioners, and breeding associations and clubs. This group has worked with 30 animal models or potential animal models during the past four years, including seven new ones recognized during this period. Some are now well established and have separate grant support including Ehler-Danlos syndrome of dogs, mink, and cats (autosomal dominant disease with defective collagen formation), combined immunodeficiency disorders in horses, and juvenile type diabetes mellitus in dogs. Other models are still in the early stages of development such as inherited feline tremors, Chediak-Higashi syndrome in cats, proliferative chondritis in rats, and inherited canine myasthenia gravis. The latter project is representative of the general approach used. A colony of approximately 50 dogs has been established. Analysis of breeding data indicates that this motor endplate disorder is transmitted as an autosomal recessive trait. The onset of the disease is early and is apparent in 8-12 week-old puppies. The clinical features are generalized muscle weakness which worsens after exercise and which improves after administration of anticholimesterase drugs. Current studies are aimed at identifying the ultrastructural features of the motor endplate, the number of endplates using a snake venom neurotoxin that binds specifically to endplates, and receptor antibody levels in the affected dogs. The latter study is being done in collaboration with an investigator at the Mayo Clinic.

Other animal model projects are oriented around selected species which have potential utility as models in more than one categorical area of research. Several marine invertebrate projects involving loliginid squid and octopuses exemplify this approach. The latter project is aimed at developing a system design and methodology for large-scale culture of octopods for biomedical research. The nervous system of the octopus is highly advanced and knowledge of the physiology and behavior of Octopus represents the most comprehensive understanding of any marine invertebrate. The great bulk of this work has been done in Europe, where O. vulgaris occurs in large concentrations that are fished commercially. In the U.S., little work has been done because none of the species occur in large, easily harvested populations along the coast. Thus, attainment of this project's goals will result in the addition of an important species to the repertoire of animals

that scientists have at their disposal for elucidating many biological principles. Results after just one year are highly encouraging. Sources of wild-caught eggs or gravid females have been found for several species, large scale culture of one species is near completion, and small scale culture of two additional species has been started. Future work will concentrate on improving system design, simplifying techniques, and on developing an array of easily-caught, cultured or manufactured food types (current diet is predominantly live shrimp.) Efforts to develop a reliable and reproducible methodology for supplying live, healthy loliginid squid for research are also progressing. Culture of Loligo opalescens from hatchlings to sexually mature adults marks the first time that a small-egged squid species has been reared in any laboratory. Future objectives include development of a standard artificial seawater squid maintenance system for use by inland research laboratories interested in the squid giant fiber system.

Special colony projects combine in varying degrees the maintenance and production of special strains or stocks of animals with ongoing research to further development and characterization of the models. Currently supported projects include a hamster resource at the University of Texas, Dallas; a bullfrog (Rana catesbeiana) resource at Louisiana State University; and a mouse mutant gene resource at the Jackson Laboratory. The latter project is typical of this group. The original mouse colony included some 140 mutants with a focus on endocrine, neurological, and immunologic problems. The specific aims are to maintain these well-defined stocks, to discover new mutations in the mouse and develop stocks of new and established mouse mutations for use as animal models in biomedical research. Over 1,750 mice were supplied to investigators last year either as breeding stock or experimental animals. A charge is made for this service and the funds are returned to the grant. New mutations kept for further study include an autosomal recessive mutation associated with an absence of fallopian tubes and uterus in the female and severe runting. Another mutation investigated during the last fiscal year is an autosomal recessive gene located on Chromosome 1 that results in an early onset autoimmune disease with generalized lymphoid proliferation and antibodies to single-stranded DNA. These mice provide an animal model applicable to human autoimmune diseases such as Systemic Lupus Erythematosus.

Support for projects related to animal model development and the establishment of special animal colonies has decreased in recent years as depicted in the following chart:

	Total Active Projects	Dollars Awarded (in 1,000's)	Percent of Budget
FY 80	24	1,912	25%
FY 81	15	1,623	23%
FY 82	12	1,055	14%

This reduction was in keeping with the Five Year Plan which provided for decreased emphasis in this area, particularly if funds were reduced for the program. The development and characterization of new models did receive

special consideration as evidenced by the one new award in this area, i.e., to develop the short-tailed opossum (Monodelphis domestica) as a laboratory animal. This marsupial, native to Brazil, appears to have many of the attributes that are desirable in establishing a laboratory species, i.e., small size, relatively docile, prolific breeder in captivity--gestation period of 14-15 days, reaches sexual maturity in 4-5 months, and is relatively free of disease and parasites. Most of these features are in marked contrast to the severe limitations of working with the Virginia opossum, the North American species most widely used to date. Marsupials are born in a semi-embryonic state roughly equivalent in development to a rat or mouse at mid-gestation. They have been particularly utilized for immunologic studies since neither thymic lymphoid tissue, peripheral blood lymphocytes nor immunoglobulins are present at birth. Their low number of large, easily identified chromosomes, neonatal capability of limb regeneration, and simple organization of many cellular and morphological characteristics make it uniquely suited for many types of biomedical research.

OTHER PRIMATE RESOURCES

In addition to the seven Regional Primate Research Centers, the Animal Resources Program supports several other nonhuman primate resources. These include two contracts and four grants for the domestic breeding of nonhuman primates. In addition, there is a grant for a Primate Supply Information Clearinghouse. These projects are part of the effort to provide a supply of primates for essential biomedical research in the face of export restrictions and embargoes by the countries of origin. The two contracts are for the production of animals for general distribution to NIH extramural investigators. As of June 30, 1982, there were 1,744 female rhesus breeders and 171 cynomolgus female breeders in the production colonies. There were 911 rhesus births and 122 cynomolgus births this past year. There were 692 rhesus monkeys and 94 cynomolgus monkeys sold from our colonies. The polio vaccine testing program did not take any animals from these colonies this year. Budget constraints are also reducing the demand for rhesus monkeys. The only requests we cannot supply yet are for young adult and adult males. Therefore, one colony of rhesus monkeys is being phased out with the expiration of the contract on December 31, 1982. This will reduce our production in the future to about one-half of the 1982 production.

The grant-supported primate breeding projects are for establishing nuclear production colonies and determining proper husbandry techniques for maintaining these colonies. Colonies under development are baboons, two species of marmosets, squirrel monkeys, and two species of Galago (bushbabies). The baboon project is the furtherest along in development. The population now includes 285 females, 40 males, 225 juveniles, and 168 infants of Papio cynocephalus and 23 females, 2 males, 9 juveniles and 16 infants of Papio hamadryas. A genetic monitoring program was recently initiated which includes development of a large battery of biochemical genetic markers for determining the extent of genetic polymorphism and parentage relationships in the founder population. Such information will provide a genetic basis for deciding which animals to maintain as breeding

stock and which best fit the needs of potential users while protecting the colony from the deleterious effects of inbreeding. In addition to these breeding and development grants, the Caribbean Primate Center at the University of Puerto Rico has a grant supporting an island colony of 900 rhesus monkeys. These monkeys have genealogy records dating back to 1938, making them very useful for social and behavior studies. The Center is also conducting some pilot studies on tropical diseases and physiology with primates housed on the mainland. The National Institute of Neurological and Communicative Disorders and Stroke maintains a colony of rhesus monkeys at the Center for fetal studies.

The Primate Supply Information Clearinghouse is designed to facilitate maximum research utilization of primates already in this country. The Clearinghouse matches requests for primates, primate tissues, and related services with investigators and breeding colonies who have these items available. The Clearinghouse publishes a weekly bulletin (circulation of 1,350) and has handled 826 formal requests for primates and 1,679 informal requests during FY 1982. From these, they placed 4,596 living primates and satisfied 123 requests for cadavers, tissues, and other specimens plus 15 cage requests. In the late summer, the Clearinghouse began to receive listings of fairly large groups of monkeys (particularly rhesus) which institutions could no longer afford to hold against future research use or breeding.

INSTITUTIONAL ANIMAL RESOURCE IMPROVEMENTS

Institutional animal resource improvement projects are awarded to help institutions upgrade their animal facilities and develop centralized programs of animal care in support of their biomedical research programs. A major objective is to enable institutions to comply with the Animal Welfare Act and DHHS policies on the care and treatment of animals. Requests of this type usually include animal cages to meet current regulations, general sanitation equipment such as cage washers, renovation of animal facilities, and addition of trained professional and technical personnel. The projects are supported for one to three years, after which time the applicant institution is expected to take over complete financial responsibility for its basic animal resource.

Institutional improvement projects have been supported since the inception of the Laboratory Animal Sciences Program. However, this area received increased emphasis in Fiscal Year 1972, when Congress appropriated an additional $1.5 million to help research institutions achieve compliance with the Animal Welfare Act of 1970 (P.L. 91-579). The NIH policy on "Care and Treatment of Laboratory Animals" (issued June 14, 1971) and the subsequent DHHS policy on "Animal Welfare" (issued May 14, 1973) also contributed to the overall response in this area. Over the past 12 years, 120 institutions have received improvement grants with awards totaling approximately $16.5 million. The following figures demonstrate the level of activity in recent years:

FY	REVIEWED	APPROVED	NEW AWARDS	TOTAL ACTIVE PROJECTS	DOLLARS AWARDED (in $1,000s)	PERCENT OF BUDGET
1971	9	5	1	14	673	11 %
1972	21	15	19	24	2,169	35 %
1973	86	62	15	28	2,318	37 %
1974	19	12	36*	46	3,217	55 %
1975	21	17	19*	38	2,582	42 %
1976	19	9	6	21	1,259	22 %
1977	14	7	6	13	1,054	19 %
1978	21	13	3	11	793	12 %
1979	9	7	4	7	709	11 %
1980	12	8	4	6	783	10 %
1981	16	16	2	7	298	4 %
1982	17	16	5	7	697	10 %

*Includes applications reviewed in previous year.

The above chart indicates a relative steady rate of new proposals in recent years. The largest number of program inquiries still touch on this area. The ability to fund new projects of other types and to combat inflationary costs has come largely at the expense of this program area. It was possible to fund five projects this year. This was due in part to assistance received from the NCI, NHLBI, NIMH, and the Minority Biomedical Support Program, DRR, which provided $225,033 for two of the improvement projects at minority institutions.

Data from the National Survey of Laboratory Animal Facilities and Resources (published March 1980; FY 1978 data) revealed the following facts relative to facilities and equipment:

- Approximately 16 percent of all nonprofit biomedical research organizations reported a need for replacement of some animal facility space now in use, 38 percent reported a need for remodeling to protect the integrity of space now in use, and 43 percent reported a current need for additional space.

- Approximately $350 million is required to meet current needs of nonprofit biomedical research organizations for space replacement, remodeling, and additions to their animal facilities. Another $407 million (using FY 1978 estimated construction costs) will be required to meet space needs projected for FY 1988.

- Nonprofit biomedical research organizations reported a current need in their animal facilities of $43 million for equipment renovation, replacement or additions.

The survey indicates in particular a need for biohazard containment space and equipment, which reflects changes in research activities and increased recognition of the need to contain hazardous agents. In order to meet needs of the scale indicated by the survey, legislative authority (new construction and major renovation) and substantial funding over a period of years would be required.

RESOURCE LABORATORIES

The objectives of these laboratories are to provide for improved animal health programs through appropriate surveillance activities and investigation of naturally ocurring disease and other laboratory animal problems, to support studies resulting in new information on diseases of laboratory animals and their etiology, to aid in the elucidation of new laboratory animal models of human disease, and to develop resources including tissues, slides, photographs, etc., for research and training. Resource laboratories have been a major program activity for over 10 years. Most resource laboratories are institutional in nature; however, in several instances it has been feasible to serve more than one institution in a metropolitian or regional area. There has been a continuing turnover in the institutions receiving such awards (support has been terminated for 14 laboratories). The total number has remained relatively constant (13-16) in recent years, and approximately 34% of the budget is awarded in this area.

Laboratory activities encompass a broad spectrum ranging from surveillance and monitoring to conduct of research on important laboratory animal disease problems. An environmental monitoring program can be very effective in demonstrating to animal care personnel the efficacy of disinfection procedures they perform and in revealing equipment malfunctions. For example, one laboratory noted no significant reduction in microbial load before and after disinfection of animal room floors. As a result, more attention was given to preparation of disinfectants and cleaning procedures. Subsequent monitoring revealed substantial improvement in this area. Rabbit watering troughs were routinely being autoclaved to eliminate Pseudomonas aeruginosa contamination. However, monitoring revealed that while the autoclave was functioning properly, it was being used incorrectly. Consequently, procedures were changed to ensure proper use. The use of detergent in the cage washer was discontinued when monitoring revealed no appreciable difference in disinfection when used.

One new laboratory was able to initiate several quality assurance projects aimed at intercurrent laboratory animal disease problems. For example, clinical case bacterial samples revealed that Pasteurella infection was the primary cause of unexpected death and illness in an 850 rabbit colony. A mandatory program requiring the purchase and maintenance of Pasteurella free rabbits was initiated campus wide. Culturing of all rabbit lungs at necropsy and of any discharges from sick rabbits has continued. Results to date indicate a reduction of 44% in the average monthly mortality and 71% in morbidity from the colony since the program was initiated.

Several institutions have relatively large flocks of sheep and goats used for research. Since Q fever has been recognized as a zoonotic hazard in animal research in other institutions, the resource laboratories have initiated surveillance programs. These studies have shown complement fixation titers for Q fever. The existence of the possible hazard has been made known to scientists and staff and preventive measures have been taken to protect laboratory and animal care personnel from exposure to sheep with potentially active infection. One institution is in the process of building new quarters for sheep and plans to gradually phase out the existing

flock and replace it with Q-fever-free animals once the new quarters are available.

Once basic monitoring and quality assurance programs are in place, the resource laboratories begin to focus on significant laboratory animal disease problems and pilot research. It is apparent that a multidisciplinary approach is necessary in order to identify and isolate etiologic agents and then take appropriate steps to eliminate or control the problem. The interaction of clinicians, virologists and pathologists was well illustrated by one resource when presented with several ill mice housed in a specific-pathogen-free barrier. An investigator was studying the effects of interferon on the response of athymic (nu/nu) mice to transplantable neoplasms. Several transplantable tumors and $100,000 worth of interferon were to be utilized for this year-long study. The pathology laboratory found morphological evidence of mouse hepatitis (MHV) infection in the sick mice which was confirmed by isolation of the virus. The tumors used in this work had previously been monitored for viral contamination and were found suitable for the experiments. The veterinary clinicans undertook a detailed epizootiological investigation of the room. They tested a number of mice in different pens serologically to determine how far infection had spread. The transplantable neoplasms also were rechecked by mouse antibody production tests but were not contaminated. During the course of their investigation, the clinicians discovered that an investigator in an adjacent room had introduced a tumor to his mice that was not premonitored and which was subsequently found to be contaminated with MHV. Further, the two investigators shared laboratory space; the presumed source of the cross-contamination. Serological monitoring of the barrier animal room revealed that MHV infection had not spread to mice on adjacent racks. Nevertheless, because the study was in its early stages, it was recommended that the room be depopulated, decontaminated and reset. The investigators were also reschooled about the dangers of MHV. Expedient detection, diagnosis and control of the infection saved this project from formidable scientific and financial hazard.

One laboratory noted occasional cases of lymphoma in chickens at necropsy. However, an apparent increase in incidence (9 of 21 chickens during a period of 10 months) prompted further studies. All cases were females procurred at one day of age. Blood samples were assayed for Marek's disease herpesvirus (MDHV) and peripheral lymphocytes yielded turkey herpesvirus and both oncogenic and non-oncogenic strains of MDHV. Investigation at the vendors revealed that the vendor normally vaccinated all birds at birth with turkey herpesvirus for Marek's disease. However, a request for non-vaccinated day-old chicks by an investigator at Washington State University had resulted in the impression that orders for day-old chicks from the University of Washington also implied non-vaccinated birds. As a result, susceptible, non-vaccinated day-old chicks were coming in contact with older birds that were shedding virus (vaccination with turkey herpesvirus prevents Marek's disease but does not prevent infection and shedding of MDHV) and after an incubation period, lymphoma developed in some chicks. Resumption of vaccination was promptly initiated to prevent additional cases of Marek's disease.

Recognition of potential animal models is an important aspect of working up problems presented to the laboratory. One laboratory discovered a mutation

in Sprague-Dawley rats with clinical characteristics of torsion dystonia (torsion dystonias are specific inherited human diseases of unknown etiology initiated by the absence of neuropathologic lesions and characterized by sustained, involuntary twisting movements). The earliest clinical signs noted at 10 days of age included a stiff paddling gait and falling from side to side. Advanced signs included complete lack of coordinated movement, hyperflexion, and rigidity. Pedigree analysis revealed both males and females were affected in a ratio indicating an autosomal recessive trait. No morphological changes were noted in histologic sections. Preliminary biochemical assays suggested widespread abnormalities in the extrapyramidal system including elevated norepinephrine levels and decreased B-adrenergic receptor binding in the cerebellar nuclei and increased dopamine receptor binding in the caudate nucleus. Psychopharmacological studies were also suggestive of biochemical abnormalities in the motor systems of the mutants. A number of important indigenous pathogens have been identified in the colony and plans are to establish a pathogen-free colony by cesarean derivation. Preliminary characterization and development of a nucleus breeding colony as a resource project has now progressed to the point that an expanded research application was submitted and recently funded by the National Institute of Neurological and Communicative Disorders and Stroke.

OTHER RESOURCE ACTIVITIES

The LASP provides partial support for the Institute of Laboratory Animal Resources (ILAR) of the National Academy of Sciences and for the accreditation program of the American Association for Accreditation of Laboratory Animal Care. The former project serves the biomedical community by providing scientific and technical information on laboratory animal resources including guidelines for their care, use and breeding; planning and conducting conferences and symposia; and promoting high quality, humane care of laboratory animals. ILAR carries out its program through a small staff and through committees of recognized experts and scientists from the scientific community. General support is also received from a number of other government agencies.

Other information projects of the LASP include support for the Laboratory Primate Newsletter and the Registry of Specialized Genetic Stocks. The latter project collects and periodically updates a "Registry" which includes listings of genetic stocks of chickens, Japanese quail and turkeys being maintained in the United States, Canada, and over 15 other countries. The most recent directory included the description and location of 209 chicken, 50 quail, and 13 turkey specialized lines and strains; inheritance, linkage and literature data; chromosome linkage maps; descriptions and location of 591 breeds and varieties; and a breeder/supplier index. Approximately 633 NIH funded research projects ($54.9 million, FY 1981) use birds.

A new project initiated in FY 1982 will result in publication of a handbook of marine invertebrate development. This handbook will provide investigators with ready access to information on methods for collection, care of adults, obtaining gametes, and maintaining a broad range of marine invertebrate species. The handbook is intended to give investigators a

broad comparative introduction to developing marine invertebrates and their use as research tools and to encourage pursuit of research on a large complex of processes and phenomena occurring in invertebrate marine animals. A second new award in the information area provided partial support for a workshop on "The Role of Animals in Biomedical Research." This workshop was cosponsored by the American Psychological Association and the New York Academy of Sciences. Held on April 28-30, 1982, in New York City, the workshop sought to inform both scientists and the public about issues that arise with respect to the use of animals for research and to assess directions that future experiments and methodologies will pursue. The proceedings will be published by the Academy and also be prepared by a science writer for release to the public.

MANPOWER DEVELOPMENT

Training in laboratory animal medicine is intended to prepare individuals to provide professional care of the many species of laboratory animals, to manage central animal resources, and to give special assistance to investigators through knowledge of laboratory animal biology and understanding of research methods. In addition, the trainees are prepared to participate in the teaching of graduate students and young investigators and to pursue their own research interests either as independent investigators or as members of a research team.

There are nine currently active training programs with a total of 31 funded trainee positions. In addition to the institutional programs, two individual postdoctoral fellowships were active at the end of the fiscal year. Since the average training period is two and one-half years, there are usually 8-10 graduates per year. Currently available figures indicate that 179 trainees and fellows have completed training since the inception of the training grants and fellowships in laboratory animal science and medicine. Sixty-three (63) of these are employed by medical schools and 69 by other academic, research or governmental organizations. The majority (105) are serving as directors or staff members of a vivarium; 59 are engaged in teaching and research or are obtaining additional training; and 15 are in public health, private practice or are retired. Retention in the field of laboratory animal medicine has been excellent, emphasizing the career orientation provided by the training and the continuing need and opportunities available for such individuals.

For the past seven years, the active training programs and diagnostic resources have been encouraged to employ veterinary students during their summer break. Ten programs and 26 students participated this past year. Critiques of the students involved were submitted to the Branch and, in turn, distributed to all the program directors. It appears that this work experience is resulting in greater knowledge and interest in the field of laboratory animal medicine by veterinary students. Several former summer students entered formal postdoctoral programs this year and development of a "pool" of such individuals for future postdoctoral training should result in long-term benefits to the field.

As the specialty field of laboratory animal medicine has matured, it has become apparent that many members of this specialty find upon completion of

their training that the demands for research resource activities have been overwhelming. Further, most recent graduates do not have the depth of research experience in a particular discipline to allow them to be competitive for regular research grants. To meet the need for additional experience and time for full-time research, a new research career development program--the Special Emphasis Research Career Award in Laboratory Animal Science--was established in FY 1982. This award emphasizes indepth experience for the laboratory animal specialist in various fundamental and clinical scientific disciplines. This special award will be made to develop multidisciplinary veterinary researchers who will direct their research toward refining the use of laboratory animals in biomedical research, the study of significant laboratory animal disease problems occurring in vivarial settings, and the development of new animal models useful in solving biomedical research problems. The first applications for this award were received June 1, 1982, and the first awards are planned for FY 1983.

ADMINISTRATIVE ISSUES

During Fiscal Year 1982 there was much activity on Capitol Hill relative to legislation which would control and attempt to reduce the use of laboratory animals in biomedical research. The Animal Resources Program was deeply involved in tracking this legislation and commenting on it. The Program also assisted in informing members of the biomedical community about the possible impact of the proposed legislation and provided biomedical research groups with available analyses for public distribution. The Program was represented at two Congressional hearings on the Walgren bill, which eventually became H.R. #6245. The Program also assisted in the drafting of comments on at least four versions of this bill.

During FY 1982 the Program received permission to establish the DRR Trans-NIH Coordinating Committee on Research Animal Resources. Its function is to coordinate activities in the area of laboratory animal science and to work collaboratively on matters concerning NIH intramural and extramural research animal resources, the care and use of laboratory animal resources, to exchange information and to provide information to the public and other agencies, and to inform and advise NIH B/I/D Directors and the Director, NIH as requested. The Committee had its first meeting on January 27, 1982, and met four times subsequently.

The Trans-NIH Coordinating Committee reviewed and made comments on the proposed NIH system of site visits to grantee institutions, suggesting criteria for these site visits and the composition of the site visit group. It reviewed the U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) system of annual reports and collaborated with USDA in reviewing their new reporting system relative to the collection of data on laboratory rodents. The Committee also reviewed with Dr. Dale Schwindaman, APHIS director, the 16 points which his group was proposing for the expansion and upgrading of their program.

The Committee heard reports on a potential DRR Biomedical Research Models Program and reports on various meetings aimed at the development of

technologies which would be alternatives to laboratory animals. It also discussed systems of review of research protocols involving laboratory animals used by other Federal agencies.

The Animal Resources Program awarded a new contract to the Institute of Laboratory Animal Resources, NAS, for a revision of the NIH "Guide for the Care and Use of Laboratory Animals." The Guide was last revised in 1978 and it was felt that a number of changes were needed, particularly in ventilation requirements, lighting requirements, and animal care services. The new contract will also specify greater input from the biomedical community and from the general public through public hearings to be held throughout the U.S. during FY 1983.

In November 1981 the Subcommittee on Primate Research Centers of the Animal Resources Review Committee (supplemented by several ad hoc members) reviewed a document entitled "Chimpanzee Guidelines" proposed by Dr. Alfred Prince of the New York Blood Center. His proposal had previously been made at the conference on Bioassay Methodology held in February 1981 in Washington, D.C. The Subcommittee concurred with most of the principles proposed regarding humane capture, special consideration of use of the animals in research, and special consideration for their care during the research procedure. The Subcommittee did not reaffirm the principles of perpetual care and housing following the primate's use in research nor did they recommend the release of the animals to the wild after their long tenure as a laboratory research subject, particularly if the animals had been born in the laboratory. The Subcommittee's report has been well received by the scientific community and by the animal welfare community.

Table I

Primate Research Centers Program Applications - FY 1982

Type	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
New.....	-	--	-	--	-	--
Renewal.....	1	3,849,160	1	3,476,110	1	3,067,474
Supplemental.....	-	--	-	--	-	--
Continuation.....	6	19,254,869	6	17,209,984	6	15,332,026
TOTALS	7	23,104,029	7	20,686,094	7	18,399,500

Table II

Laboratory Animal Science Program Applications - FY 1982

Type	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
New.....	47	5,487,555	43	3,813,575	13	1,158,388
Renewal.....	14	2,023,710	14	1,610,533	5	808,655
Admin Supplement...	11	260,971	11	260,971	11	359,481
Competing Suppl'mt.	1	12,955	1	7,239	-	--
Continuation.....	33	4,211,649	33	3,317,988	32	4,282,989
Continuation (J-2).	1	11,070	1	11,070	1	14,834
TOTALS	107	12,007,910	103	9,021,376	62	6,624,347

Table III

Laboratory Animal Science Programs - FY 1982

Programs	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
Resource Research..	21	1,618,535	18	1,154,552	11	621,286
Primate Resource...	9	1,248,697	9	961,055	6	1,093,973
Colonies & Models..	20	1,630,878	20	1,354,573	11	1,048,287
Basic Improvement..	19	3,476,599	18	2,401,870	7	696,835
Diagnostic Labs....	18	2,863,854	18	2,133,539	14	2,428,618
Reference.....	7	772,170	7	637,202	5	437,777
Information.....	11	325,181	11	310,589	7	258,821
Research Career....	-	--	-	--	-	--
New Investigator...	2	71,996	2	67,996	1	38,750
TOTALS	107	12,007,910	103	9,021,376	62	6,624,347

1/ Direct Costs Only.
2/ Includes Indirect Costs.
3/ Includes Reimbursable Funds ($65,000) from NIA.
4/ Includes Reimbursable Funds ($30,000) from NIMH for Co-Funding One New Project, but Does Not Include Co-Funding Funds ($137,900) Awarded By NCI ($70,000), and NHLBI ($67,900) for Two New Projects.

Table IV

Contract Program - FY 1982

Program	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
Colonies & Models..	1	6,891	1	6,891	1	6,891
Primate Supply.....	2	424,262	2	424,262	2	374,262
Other Prog Activ...	2	126,000	2	126,000	2	126,000
TOTALS	5	557,153	5	557,153	5	507,153

Table V

National Research Service Award Program - Institutional - FY 1982

Type	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
New.....	4	169,595	4	169,595	1	62,914
Renewal.....	5	586,696	5	577,566	4	332,456
Admin Supplement...	1	125,232	1	115,302	1	63,044
Continuation.....	3	333,213	3	380,585	3	168,045
TOTALS	13	1,214,736	13	1,243,048	9	626,459

Table VI

National Research Service Award Program - Individual - FY 1982

Type	Number Rec'd	Amount Requested	Number Appr	Amount Approved	Number Funded	Amount Funded
New.....	1	21,780	1	21,780	1	21,780
Renewal.....	-	--	-	--	-	--
Supplement.....	-	--	-	--	-	--
Continuation.....	1	17,736	1	17,736	1	17,736
TOTALS	2	39,516	2	39,516	2	39,516

Table VII

Short Term Training Program Applications - FY 1982

Type	Number Rec'd	Amount Requested 1/	Number Appr	Amount Approved 1/	Number Funded	Amount Funded 2/
New.....	1	26,130	1	26,130	-	--
Renewal.....	-	--	-	--	-	--
Supplement.....	-	--	-	--	-	--
Continuation.....	1	12,060	1	12,060	1	13,025
TOTALS	2	38,190	2	38,190	1	13,025

1/ Direct Costs Only.
2/ Includes Indirect Costs.

Table VIII

Summary

Type	Number Rec'd	Amount Requested[1/]	Number Appr	Amount Approved[1/]	Number Funded	Amount Funded[2/]
I.....	7	23,104,029	7	20,686,094	7	18,399,500
II and III...	107	12,007,910	103	9,021,376	62	6,624,347
IV.....	5	557,153	5	557,153	5	507,153
V.....	13	1,214,736	13	1,243,048	9	626,459
VI.....	2	39,516	2	39,516	2	39,516
VII.....	2	38,190	2	38,190	1	13,025
TOTALS	136	36,961,534	132	31,585,377	86	26,210,000

1/ Direct Costs Only.
2/ Includes Indirect Costs.

Fiscal Year 1982 Annual Report
Biotechnology Resources Program
Division of Research Resources

INTRODUCTION

The Biotechnology Resources Program (BRP) was initiated in 1962 in response to a Congressional interest that NIH establish an activity focused on specialized equipment needed for biomedical research. Since that time, the BRP (formerly called Special Research Resources has modified and expanded its scope. While the Program in the early years mainly supported large general purpose computer centers in medical schools, it later moved into an extremely broad and innovative array of biomedically relevant technologies. In addition, the Program now places greater emphasis on regional and national sharing of resources. Major thrusts of the Program today are applications of knowledge engineering, information technology, biomedical engineering and digital technology to biomedical and clinical research programs, and technologies for the study of biomolecular and cellular structure and function.

RESEARCH ACCOMPLISHMENTS

Knowledge Engineering and Information Technology

Expert Systems - The Rutgers University Resource on Computers in Biomedicine under the direction of Dr. Saul Amarel, Principal Investigator, developed a system which has many of the dynamic characteristics needed to produce easily updatable computer models of clinical reasoning. SEEK (System for Empirical Experimentation with Expert Knowledge) provides the builder of a medical consultation model with the tools needed to test its reasoning against a database of cases with well established diagnostic and therapeutic end-points. It adds a number of features that makes building such models easier for the physician or biomedical researcher who is only slightly familiar with computers. SEEK prompts the model builder to enter the description of diagnostic rules in the form of a table, where each disease or clinical condition can be defined in terms of the classical medical terminology of major and minor findings, as well as necessary requirements for the diagnoses and the conditions that might exclude or rule them out. Each diagnostic category can have levels of confidence attached to it, such as definite, probable and possible, to account for the uncertainties and ambiguities of data and decisions. SEEK is the first knowledge based system of its kind. It should become progressively more valuable as computer memory sizes increase. It provides the medical researcher with the tools needed for clinical testing of a knowledge base with realistic size models and numbers of clinical cases.

The staff at the Rutgers University Research Resource have also developed an "expert" program that has been incorporated in a commercial instrument. This is a Serum Protein Diagnostic Program which simulates the reasoning that a pathologist or clinician uses

to interpret a serum protein electrophoresis pattern. This frees up valuable time that can be devoted to complex tasks that do not lend themselves to computerization. Helena Laboratories Corporation is the first company offering a complex knowledge engineering system in a laboratory instrument of their CliniScan densitometer/analyzer.

Display of 3-D Biomedical Images - A new computer-based, true 3-D display system has been designed to display new kinds of 3-D biomedical image information at the Resource at the Mayo Foundation, Dr. Richard Robb, Principal Investigator. The new image data is a consequence of the development of computed tomographic (CT) scanners capable of producing images of multiple parallel thin sections through the body. An individual CT scan is a two-dimensional array of numbers called picture elements (pixels for short) which is usually displayed on a television monitor. The display device converts the 2-D array of numbers into a 2-D distribution of brightness. A "stack" of CT images is referred to as a volume image, and is a 3-D array of volume picture elements (voxels for short). The new display device extends the concept of a 2-D distribution of brightness into the third dimension. The device uses a conventional display monitor and a moving optical element which in this case is a membrane mirror stretched over a loudspeaker. Individual CT images in a stack are displayed one at a time on the face of the display mirror in synchrony with the mirror position. The first image appears furthest away, the second somewhat closer, i.e., just in front of the first image, and so on until all the images have been displayed. Although only one image is displayed at a time, they are displayed in rapid sequence relative to the visual integrating time of the human eye-brain combination, so that the images appear simultaneously as a stack behind the mirror. The resulting image looks like a 3-D X-ray of the entire object. The system is designed so that the observer can "cut" or "peel" away overlying image regions (structures) to peer inside and study 3-D anatomy. The system allows the investigator to interact with the image data much like the surgeon or pathologist interacts with the body or tissue samples. However, image manipulation is done non-invasively and non-destructively, permitting repeated detailed and accurate quantitative examination and measurement of body organs and tissues in health and disease.

Axonal Regeneration - Under What Conditions Do Regenerating Axons Grow Back To Their Original Location In the Brain? - During embryonic development of the nervous system, the axons of nerve cells grow to specific regions and form connections with other nerve cells. In many animals, axons retain the ability to grow even in the adult, so that if an adult nerve is severed the axons grow again and re-establish connections with other nerve cells. The extent and accuracy of regeneration determine how well function is recovered. One way for this to occur would be if axons grow back to exactly the same locations they occupied before. Alternately, axons might grow into the generally appropriate region but still manage to find the original targets at somewhat different locations in the brain. Lastly, if the severed part of the axon survives, then the growing

tip of the axon might recognize it and fuse with it, thus directly reestablishing itself at the same positions it had earlier.

The Resource at Columbia University under the direction of Dr. Cyrus Levinthal, Principal Investigator, is working with scientists at the Carnegie Institution of Washington. Using a technique developed at Columbia for observing pairs of cells filled with different dyes simultaneously, they have found that all of these regenerative mechanisms are used by nerve cells in the nervous system of the medicinal leech. Through the use of CARTOS, a computer based system developed at the Columbia Resource for 3-dimensional reconstruction of images from serial sections, the scientists from Columbia and the Carnegie Institution have reconstructed individual nerve cells filled with an opaque dye at various times after their axons are severed. By filling another cell in the region where the axon is growing with a flourescent dye, the research scientist can observe whether the axon grows back to its original location or whether it goes off to unusual regions. Both of these possibilities occur.

In addition, in a small fraction of the experiments and at very short times after surgery, a completely normal axon is found, indicating that it has connected back to itself. In all cases it is found after a sufficient long time has elapsed, that normal connections, measured electro-physiologically, return. Thus, regeneration is a complex phenomenon, with function returning even if the regenerating nerve cell is anatomically different from what it was earlier.

Arterial Wall Catabolism of Lipoproteins in vivo and the Early Vascular Alterations in Hypertension - It is a well recognized phenomenon that blood vessels are not completely impermeable to elements circulating in the blood stream and that permeability changes occur in hypertension. Thus, for the past 30 years people have proposed that the reason there is an increase incidence of atherosclerosis in hypertension is that the increased blood pressure filters out into the wall of the blood vessels, an increased amount of lipids and lipoproteins. These assumptions have been tested by measuring the transport properties of rabbit aorta and looking at specific entry, accumulation, and removal of low density lipoprotein by studying the kinetics of plasma tissue exchange of lipoproteins labeled with radioisotopic iodine. Studies following a single injection of the radiolabeled lipoprotein allows calculations of the endothelial permeability, the diffusion coefficient and the amount of lipoproteins degraded in the aorta by metabolism. Changes in these parameters are then studied in a series of animals with experimental hypertension where both lipoprotein and albumin permeability are measured. Scientists at the Cleveland Clinic Foundation are obtaining this data experimentally and are then using the PROPHET National Computer Resource to develop mathematical models to measure the rate of influx of these large proteins, to measure their rate of accumulation inside the aorta, and to measure their rate of metabolic breakdown within the aorta. From the mathematical models, derived rate constants can then be determined and the suitability of applying these back to the experimental

condition determined. One can distinguish permeability coefficients, diffusion coefficients and degradation rates in both normal animals and animals with hypertension. This in turn will allow one to predict a little more accurately whether one can alter the increased incidence of atherosclerosis and thus myocardial infarcts
in patients with hypertension and whether different types of hypertension may have differential effects on the degree of atherosclerosis.

Biomedical Engineering and Digital Technology

Chemical Sensors - The Biomedical Electronics Resource at the Case Western Reserve University under the direction of Dr. Wen H. Ko, Principal Investigator, is conducting a very active program of research and development in the ion sensitive field effect transistor (ISFET) sensor. Resource investigators have been able to produce reliable and functional ISFET sensors for the measurement of acidity (pH), potassium ions, calcium ions, and others, which represent some vital electrolytes in the body. They are currently starting to apply some of these new sensors produced in their laboratory clinically. One of the first clinical studies started is the use of their pH-sensitive ISFET sensor for gastrointestinal reflux study. They have successfully fabricated a small diameter esophageal probe with four to five individual pH-ISFET sensors placed at the distal end of the probe. These sensors are placed approximately two to three centimeters apart from each other. The significance of this linear array of sensors along the probe is that information on the level of the gastric reflux can be obtained. This method is in contrast to the current method where one miniature sized glass pH electrode is placed at the very end of a probe. Therefore, through this probe, both the magnitude of the pH reflux and the height to which the reflux rises can be obtained through the array sensor design.

They have applied this probe with ease to several adult patients and have confirmed the accurate functioning of our sensors. Acidities of the stomach juices from pH 1 to pH 6 have been observed. The rapid response of these sensors will also insure the ability to record the fast rising reflux. Their clinical collaborators are encouraged and are in the process of instituting the use of this probe as a routine diagnostic test in their gastrointestinal reflux diagnostic procedure. They are also initiating tests of this probe in infants where it can provide significant information concerning abnormal feeding habits of the infants. Another potentially significant application of this probe is for the monitoring of newborns thought to be susceptible to sudden infant death syndrome (SIDS) for the recent clinical evidence has suggested that SIDS may be related to abnormal gastrointestinal reflux.

Force Transducer and System for the Study of Bone Joint Forces - The measurement of forces generated at the articulating surfaces between bones during normal activity has been difficult because there was no transducer that allowed minimal interference with normal function.

A unique method for measuring these forces has been implemented at the Biomedical Electronics Resource at Case Western Reserve University. It will be of value to researchers in the fields of orthopedics, orthodontics and similar disciplines.

By encapsulating a metallized piezoelectric polymer (i.e., polyvinylidene flouride: PVDF) in teflon, a force transducer with a thickness of less than 15 mils (0.38mm) can be fabricated. The material lends itself to cutting into virtually any width, length or shape for implantation. Since the resulting transducer is flexible, it can easily conform to irregular surfaces. To stabilize the implant, the teflon surface may be etched and then cemented to the experimental surface. After a suitable impedance shifting network, the force signal can be coupled to implantable telemetry systems directly wired to readout devices.

A free-roaming animal study was done on the temporomandibular joint (TMJ) in collaboration with Dr. Charles Gibbs, College of Dentistry, Division of Fixed Prosthodontics, University of Florida, Gainesville, Florida, using a PVDF transducer tailor-cut for the TMJ and linked to the M7-K6 telemetry system. Useful data were collected for the study of forces developed during mastication.

Brain Studies with Positron Emission Tomography (PET) - The brain functions on the basis of an extremely complex interaction between biochemical and physiological processes, distributed throughout the organ. These processes are continually changing with the normal activity of the brain. Although it is possible to study such processes in living animals as well as in isolated systems, it has been difficult to apply the information to man in vivo. Because the functions of the brain are unique to the human and because it has been impossible to create animal models of many diseases afflicting the nervous system of man, the development of PET assumes special importance. PET provides a means to directly quantify local biochemical, metabolic and hemodynamic changes in the human brain noninvasively.

PET represents a remarkable collaboration among investigators of diverse disciplines. The development of radiation-detection strategies and image-reconstruction techniques have required the combined efforts of engineers, computer scientists, applied mathematicians and physicists. Somewhat less obvious have been the major efforts of applied mathematicians, neurologists and computer scientists devoted to the development of quantitative tracer techniques that now permit the use of PET in a meaningful way for clinical investigation. During the past several years scientists at the Washington University Computer Resource under the direction of Dr. Lewis Thomas, Jr., Principal Investigator, have developed strategies for the measurement of local cerebral blood volume, blood flow, oxygen consumption, glucose utilization, tissue pH and neuroreceptor pharmacology. Currently under development are techniques for the measurement of local protein synthesis and tissue lipid content.

The Washington University scientists are presently applying PET techniques in several clinical studies. Measurements of local blood flow, blood volume and oxygen consumption are being used in patients with symptomatic ischemic cerebrovascular disease (threatened stroke) in order to identify those who would benefit from reconstructive vascular surgery. PET studies appear to be uniquely suited to this task. They are also employing PET to identify local areas of abnormal metabolic activity in the brains of patients with intractable epilepsy. Such informtion is invaluable in determining the feasibility of surgical intervention. PET is being used to identify unique metabolic changes within the brains of patients with movement disorders such as Parkinson's disease and to study the manner in which the brain processes incoming auditory information. These studies are a prelude to studies designed to better understand a number of perceptual disorders encountered in neurology.

Treatment of Idiopathic Scoliosis - Dr. Neal E. Miller and Dr. Barry Dworkin, behavioral scientists at Rockefeller University, assisted by staff and Principal Investigator, Dr. Robert L. Schoenfeld, of the Microprocessor Biotechnology Resource, have developed a method to treat idiopathic scoliosis by employing the techniques of biofeedback. (Dr. Dworkin is now continuing this work at Pennsylvania State Medical College). Scoliosis, untreated, usually ends in lateral curvature of the spine and can result in severe deformity and, in some cases, death. Historically, scoliosis has been treated by having the patient wear a cumbersome, movement-restricting Milwaukee brace or by surgery. A more recent treatment involves electrical stimulation of paraspinal muscles through implanted coupled coils or transcutaneous stimulation of trunk musculature by external stimulation. The patients in this project wear a lightweight (6 oz.), small, battery-powered device which detects undesirable posture shifts by means of two flexible nylon cords placed about the torso in a horizontal and vertical plane. A miniaturized electric circuit uses digital logic to respond to these postural shifts. After a preset time delay, an audio-oscillator turns on at low volume so that a faint tone is heard by the patient. Correction of the improper posture turns off the oscillator. Failure to correct the posture shift in a certain time interval will produce a much louder tone.

In addition, certain "memory" features have been provided. The purposes are to discourage the patient from staying out of proper posture for time intervals just short of that required to produce an audible tone, and to reward the patient who maintains proper posture for long time intervals by lengthening the delays which receive audible tones. Since 1973, 12 patients have been treated in New York City. Ten of these patients have successfully completed treatment with a -8% net change in curvature (on average), one withdrew from treatment after six months, and one switched to a more conventional treatment after failing to progress after an initial successful period of treatment. Preliminary results from other treatment groups both in the United States and in Germany are consistent with the results obtained in New York.

Technologies for the Study of Biomolecular and Cellular Structure and Function

Fast Atom Bombardment Mass Spectrometry - The Massachusetts Institute of Technology Mass Spectrometry Facility under the direction of Dr. Klaus Biemann, Principal Investigator, has added a new capability to its range of techniques availble for analyses of complex samples. The new method, called Fast Atom Bombardment (FAB) allows researchers to examine very polar and very high molecular weight materials, to determine their molecular weights and structures. Since many of the most important biological molecules such as proteins and antibiotics can be analyzed more easily, FAB has extended the utility of mass spectrometry in these areas. Many compounds which have high activity such as endorphins, bacterial cell wall components or pheremones are available in only very small quantities. Techniques such as FAB, which require much less chemical manipulation during the workup procedures than do the more traditional methods, are the only practical way to do structural determinations on the amounts of material which it is feasible to prepare. Other mass spectrometry Resources will also have FAB capability.

Porphyrin Sensitized Cells - Porphyrin derivatives are naturally-occurring molecules which have the property of sensitizing cellular systems to interaction with visible light. This interaction can result in damage (often lethal) to the cell. In certain intances such damage can be deleterious, for example in erythropoetic porphyria; in other circumstances this ability to cause biological damage can be beneficial, as for example in the sensitized killing of tumor cells by visible light. Photodynamic effects possibly proceed by complex chain of reactions initiated by photon absorption in the porphyrin molecule. One possible subsequent intermediate species is an electronically-excited form of oxygen (singlet oxygen) which is formed through a collisional interaction between the photo-excited porphyrin and normal oxygen molecules. Dr. M.A.J. Rodgers of the Center for Fast Kinetics Research, University of Texas, which is directed by Principal Investigator Dr. Edward L. Powers, in collaboration with Drs. Jori and Redd of the University of Padua, Padua, Italy, are testing this hypothesis and attempting to quantify the several reactions which can affect the efficiency of the process. In the applications area Dr. Michael Berns, Principal Investigator of the Laser Microbeam Biotechnology Resource at the University of California, Irvine, has recently demonstrated, in collaboration with physicians from the medical school, that laser light in conjunction with porphyrin derivatives can be used to eliminate or cause regression of several types of malignant tumors. Some porphyrin derivatives have been found to concentrate in tumor tissue, and irradiation of treated patients with laser light of the approprite wavelength either directly for surface tumors or using a fiber optic catheter for deeper lesions induces a photochemical reaction which leads to rapid cell death. Of the 38 irradiated breast tumors in 10 patients used in initial studies, a majority underwent necrosis or major

regression of the tumor mass within 14 days. Further studies are underway.

Protein Crystallography - The X-ray diffraction data collection system for protein crystals at the Biotechnology Resource at the University of Virginia, Charlottesville, is in the final stages of development and should be available to users within the coming year. Dr. Kretsinger, Principal Investigator, and Dr. Sobottka have collected test data for several proteins on the multiwire area detector diffractometer, and are evaluating this data and modifying the software for easy use by outsiders. A film-based oscillation camera X-ray data collection system is being developed at the Stanford University Synchrotron Radiation Biotechnology Resource, Dr. Arthur I. Bienenstock, Principal Investigator, and should also be available within the next year.

WORKSHOPS, CONFERENCES AND EXHIBITS

The Workshop at the University of Pittsburgh, August 16-17, 1982 on Artificial Intelligence in Medicine (AIM) focused on the critical issues unearthed as a result of the first decade of AIM research. Participants included experts outside the AIM community from academia, industry, foundations and government. The results of the workshop included:

- identification of needs for breakthroughs in AI technology
- identification of impact of technological innovation in hardware
- the issue of the reward systems in interdisciplinary research
- an assessment of benefits and costs of expert systems and
- addressed the decision on whether or not to collaborate intensively with Japan in their commitment to develop expert systems in medicine.

A workshop at Aspen, Colorado August 30 to September 17, 1982, sponsored by the BRP, aimed at extending the range and power of computational insight in molecular genetics. This work dealt with both representation in the computer of genetic relationships and with computational aids for assessing the significance of new relationships. Appropriate roles of computers ranging from microcomputers to large scientific computers was examined.

The PROPHET Resource held its annual Users' Colloquium on May 12-14, 1982. The PROPHET System is a time-sharing computer system designed to meet data analysis needs of biomedical researchers. The project operates under contract with Bolt Beranek and Newman, Cambridge, Massachusetts. Scientists with minimal familiarity with computers can use PROPHET using English-like commands. Extensive capabilities are available for data

manipulation, mathematical modeling and statistical analysis. Users can create and analyze models of molecular structures which may be displayed in a variety of ways. A programming language is available which permits users to write their own procedures and functions to suit particular needs. Users of PROPHET meet annually at the Users' Colloquium, held this year at Airlie House, Airlie, Virginia.

Topics presented at the Colloquium included the Human Modeling and Simulation Program, the Chemical Substances Information Network, use of PROPHET for applications of molecular mechanics, PROPHET applications at the Seattle Primate Center, an interactive procedure for superimposing structures of small molecules in PROPHET, and the use of PROPHET by the FDA in the drug approval process. Eight special workshops were held and three special interest groups met. The Molecules Special Interest Group, Statistics Special Interest Group and the Modeling Special Interest Group met to develop user recommendations for future developments.

A workshop was held in Cambridge, Massachusetts on July 27-29, 1982 at the site of the PROPHET contractor to obtain input from the PROPHET user community regarding new and emerging terminal technologies. Among the topics discussed were applications of intelligent terminals and the need for enhanced graphics. The workshop participants included representatives from PROPHET's academic, government and commercial user groups. The workshop was held in conjunction with the Association for Computing Machinery's Special Interest Group on Computer Graphics annual conference and exhibition held in Boston at the same time. Workshop participants attended conference sessions and viewed the exhibits which presented the state-of-the-art in graphic terminals and systems. Bolt Beranek and Newman will present a report to the BRP based upon the workshop discussions which will indicate opportunities presented by new terminal technologies to enhance the PROPHET Network's capabilities.

A workshop on Time-of-Flight Emission Tomography was held at Washington University on May 17-19, 1982. Approximately 60 invited scientists attended, including scientists from France and Japan. Session topics included Biological Motivations, Systems under Development, Event Detection Technology, Algorithms for Reconstruction and Design Considerations for Data Acquisition and Processing. For each session, a chairman and discussion leader developed consensus reports which were reviewed and approved by the Workshop participants in a concluding plenary session. A presentation of the Washington University SUPER PETT time-of-flight system was also included. The proceedings of the conference will be published by the IEEE Computer Society. Funding was supplied by BRP, NHLBI, IEEE Computer Society, the Hamamatsu Corporation, Nucletronix, Scanditronix and by the Washington University School of Medicine (Mallincrodt Institute of Radiology and Biomedical Computer Laboratory).

The International Workshop on Blood Gas Sensor and Measurement Technology held June 14-17, 1982 in Columbia, Maryland was the tenth

in a series covering applications of technology to biomedical research and clinical medicine. In addition to the usual sponsorhip by the Biomedical Electronics Resource at Case Western Reserve University and the BRP, seven industrial co-sponsors were involved for the first time in this series.

The BRP co-sponsored a Gordon Conference on Diffraction Methods in Molecular Biology in July of 1982. The Conference covered recent advances in proteins and nucleic acid structure analysis based upon X-ray crystallography, electron diffraction, and computational approaches to structure prediction and analysis. An overview of results and capabilities of synchrotron based X-ray studies was also presented.

The BRP provided some funds in support of the Xth International Conference on Magnetic Resonance in Biological Systems at Stanford University. Topics included NMR of cells and tissues, NMR imaging, enzyme and protein studies and membrane studies.

The Program also partially supported the First Annual Conference of the Magnetic Resonance Imaging Society in Boston, Masschusetts. The Conference covered both basic and clinical science, and included papers on NMR imaging, in vivo spectroscopy, mathematical aspects of reconstruction, ESR, contrast imaging agents for NMR, and workshops on basic and clinical applications.

The BRP showed an exhibit featuring the Resource Directory and Program Guidelines at the Fifth Symposium of Computer Applications in Health Care, November 2-4, 1981, Washington, D.C.

PROGRAM DEVELOPMENTS

Small Grant Program

The Program initiated a small grant award beginning with the February 1, 1983 application receipt date. This is a one-year non-renewable award for maximum of $15,000 for pilot projects in high technology and engineering related to biomedical research. The awards are for projects which involve feasibility studies of innovative and high risk ideas and provide a basis for more extended research in the project's technology. The purpose of the small grant awards is to enable examination of a new technology for its usefulness in biomedical research, develop significant changes in an existing technology important to biomedical research or translate scientific notions into a basis for a future technology for biomedical research. BRP expects to make approximately 10 to 20 awards for Fiscal Year 1983, contingent on receipt of meritorious applications and appropriated funds.

New Grants Awarded - BRP funded six new resource grants this year. A Resource for the study of metalloenzymes, proteins and model compounds using synchrotron radiation from the National Synchrotron Light Source was funded with Dr. Britton Chance as the Principal

Investigator. The Resource will initially emphasize extended X-ray absorption fine structure analysis capabilities and anomalous X-ray scattering studies. It is located at the National Synchrotron Light Source at Brookhaven National Laboratories and the University of Pennsylvania.

A National Flow Cytometry and Sorting Research Resource under Dr. L. Scott Cram, Los Alamos National Laboratory was initiated. In addition to collaborative and service aspects of research involving cell sorting, the Resource will be developing several specialized capabilities for cell biology research. These include a chromosome sorting instrument, advanced multi wavelength sorter and a project to extend the use of fluorescence polarization and energy transfer in biology to flow cytometry where mixed populations of cells could be rapidly characterized using these parameters.

An ultrafast Optical Processes Laboratory under Dr. Robin Hochstrasser, University of Pennsylvania, has been funded to augment the existing National Science Foundation Regional Laser Laboratory so that picosecond optical techniques can be effectively employed to study biological processes. The Resource will emphasize development of two major instruments: a high speed fluorescence spectrometer and a picosecond time-resolved Raman spectrometer.

A National Tritium Labeling Facility was funded at the Lawrence Berkeley Laboratory under Dr. Richard M. Lemmon. The facility will do research on labeling methods, and provide high activity labeled biological compounds not otherwise available for biomedical research applications.

A resource for detecting and mapping very small electric currents in cells was established at the Marine Biological Laboratory, Woodshole, Massachusetts, with Dr. Lionel Jaffe as principal investigator. This resource will permit investigators to study the electric currents generated at the surface of living cells in a non-invasive manner.

A Resource for Biomedical Computing with Dr. Lewis J. Thomas, Jr. as principal investigator continues the activities of a resource at Washington University which has had a long and important history in developing both hardware and software tailored to biomedical needs. This Resource was reclassified as a new or Type 1 grant because of significant changes in both technology and science. Included in the new areas of this grant are: (a) the development of an enhanced version of a positron-emission transaxial tomography scanner using high speed signal acquisition and preprocessing to incorporate time-of-flight data, (b) the development of an improved image processing system for accurate analysis of radioautographs, and (c) the development and evaluation of a system for the early recognition of visual defects in glaucoma.

Three new resource-related research projects were funded this year. A resource development activity entitled "Computer Systems for Optimal Control and Dosage Regimens" was funded at the University of

Southern California. Dr. Jelleffe, the Principal Investigator, and his collaborators plan to develop a hand-held computer system which determines optimum dosage levels of drugs for individual patients.

A resource-related research project in Very Large Scale Integrated Circuits for Biomedical Applications was funded at Washington University with Dr. Charles E. Molnar as Principal Investigator. The investigators in this project will develop VLSI systems with synchronous technology. Another resource-related research project awarded to Washington University will investigate quantitative ultrasound imaging of human tissues for use in clinical identification of tissue pathologies.

Administrative Issues

The possibility of limiting the length of a resource center grant award to 10 years or two project periods was examined by Program staff, Biotechnology Resources Review Committee and the Council Program work group. Such a limit would assure turnover of resources and funding of new emerging technologies. Although turnover of resources is important and is occurring, the time to terminate resources will vary with the nature of technologies. Instead of placing an arbitrary limit of 10 years on grant awards, the Program will change its guidelines to indicate resource technologies must be at the forefront of science. Once a resource's activities primarily involve service and collaborative projects, its support should be derived from the user community and sources other than BRP. This stage in the life of a typical resource is usually 10 years.

The review of BRP grant applications has been slightly modified this past year to accommodate the heavy review schedule of the Special Review Section, Division of Research Grants. In place of the parent special study section which reviewed BRP applications, special study sections for each application are established. Continuity in the review of applications will be established by using a group of experienced reviewers on the special study sections and generally to have some reviewers participate on more than one special study section per cycle. In addition, the Biotechnology Resources Review Committee reviews the summary statements and makes recommendations to Council on Program relevance based on BRP policies and priorities.

USE OF BIOTECHNOLOGY RESOURCES

One of the primary measures of accomplishment that can be applied to BRP is the extent to which its sponsored resources assist the various NIH categorical programs. With their cadres of highly skilled staff scientists and their specialized and often unique facilities, Biotechnology Resources are frequently the scene of productive encounters between experts in given technology and experts in a given biomedical discipline. Table I lists the number of PHS grants that made use of Biotechnology Resources and awarded dollars to these grants. The distribution of research assisted by

the BRP reflects in part apportionment of research funds to the NIH Institutes and other agencies.

The total number of projects in Biotechnology Resources and the number of investigators which made use of Biotechnology Resources are given in Table II for Fiscal Years 1979, 1980, and 1981. The number of publications resulting from research projects conducted in Biotechnology Resources in Fiscal Years 1979, 1980, and 1981 are also given in Table II.

EXPENDITURES BY CATEGORY

The Program supported resource grants, resource-related research project grants, new investigator research awards, conference grants and contracts during FY 1982. The varied technologies the Biotechnology Resources provide are classified as follows:

Type	Number	$ Awarded FY 1982
Knowledge Engineering and Information Technology		
Knowledge Engineering	6	2,945,697
Information Technology	7	1,833,102
Biomedical Engineering and Digital Technology		
Biomedical Engineering	3	1,377,158
Digital Technology	6	2,433,090
Technologies for Study of Biomolecular and Cellular Structure and Function		
Biomolecular Structure and Function	22	6,074,324
Cellular Structure and Function	10	3,055,142

The aggregate annual level for the grant and contract activities is approximately $20 million. A list by Program category of BRP-sponsored grants and contracts is given in Table III, together with brief descriptions of the capabilities and research emphasis or applications for each.

TABLE I
PHS Support for Investigators
Using Biotechnology Resources for FY 1980

NIH Institutes	Number of Grants	Awarded Dollars in $1,000
Aging	6	724
Allergy and Infectious Diseases	44	4,130
Diabetes, Digestive Diseases and Kidney	149	15,066
Cancer	171	19,127
Child Health and Human Development	42	4,418
Dental Research	7	472
Environmental Health Sciences	17	3,337
Eye	43	3,799
General Medical Sciences	299	32,592
Heart, Lung and Blood	127	21,084
National Library of Medicine	7	1,171
Neurological and Communicative Disorders and Stroke	52	4,918
Fogarty International Center	5	106
Division of Research Resources	22	3,924
Total NIH	991	114,867
Other PHS Components		
Alcohol, Drug Abuse and Mental Health Administration	36	3,158
Health Resources Administration	4	461
Center for Disease Control	1	128
Food and Drug Administration	1	24
Office of Health Research, Statistics and Technology	4	423
Total PHS	1,036	119,038

TABLE II
Use and Publication Records of Biotechnology Resources

	FY 1979	FY 1980	FY 1981
Number of Projects	1,421	1,346	1,938
Number of Investigators	2,088	2,180	3,104
Number of Publications			
Papers	863	829	1,722
Books	87	76	84
Abstracts	232	241	309
Total	1,182	1,146	2,115

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Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
I. Knowledge Engineering and Information Technology in Biomedicine						
A. Knowledge Engineering						
3 R24 RR 00612-12S1 5 R24 RR 00612-13	Carl Djerassi, Ph.D. Stanford Univ. Stanford, Ca.	Resource-Related Research: Computers and Chemistry	Computer software for interpretation of mass spectrometry data	Development of techniques for computer-assisted molecular structure elucidation	28,777 269,229	4,010,034
5 P41 RR 00643-11	Saul Amarel, Sc.D. Rutgers Univ. New Brunswick, N.J.	Research Resource on Computers in Biomedicine	Access to time-sharing systems	Application of artificial intelligence to clinical decisionmaking and medical modeling	610,741	5,283,085
3 P41 RR 00785-09S1 5 P41 RR 00785-10	Edward A. Feigenbaum, Ph.D. Stanford Univ. Stanford, Ca.	S U Medical Experimental Computer Resource (SUMEX)	Remote access through computer networks	Biomedical research applications of artificial intelligence and computer sharing for health research	11,060 1,215,105	9,956,882
3 R24 RR 01101-05S1 5 R24 RR 01101-06	Harry E. Pople, Ph.D. Univ. of Pittsburgh Pittsburgh, Pa.	Clinical Decision Systems Research Resource	Computer-based diagnostic consultation systems	Artificial intelligence methodology for clinical decision systems	63,012 354,552	1,758,123
3 P41 RR 01243-01S1 5 P41 RR 01243-02	James B. Bassingthwaighte, M.D., Ph.D. Univ. of Wash. Seattle, Wash.	Resource Development Program in Simulation Analysis	Computer simulation systems	Development of simulation methods, software and hardware systems in micro circulation and cardiovascular research	16,000 158,649	329,190

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Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
		I. Knowledge Engineering and Information Technology in Biomedicine				
A. Knowledge Engineering (continued)						
1 R13 RR 01341-01	Nicholas H. G. Holford, Ph.D. Univ. of California San Francisco, Calif.	The PROPHET Modelling Workshop		A review of current major computer-based modeling systems and future needs in modeling	--	27,322
1 R24 RR 01629-01	Roger W. Jelliffe, M.D. Univ. of Southern California Los Angeles, Calif.	Computer Systems for Optimal Control of Dosage Regimens	On line real time control of dosoage regimens	Development of ootimal Bayesian feedback dosage strategy	218,679	--

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Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
		I. Knowledge Engineering and Information Technology in Biomedicine				
B. Information Technology						
5 R24 RR 00007-19	Richard A. Robb, Ph.D. Mayo Foundation Rochester, Minn.	Computer Analyses of Biosystem Structures and Functions	Image processing and analysis	X-ray, ultrasound and non-invasive monitoring of radionuclide imaging of major organs of the body	280,316	7,637,752
2 P41 RR 00442-14	Cyrus Levinthal, Ph.D. Columbia Univ. New York, N.Y.	Computer Resource for Image Processing and Display	Image processing and interactive graphics	Neuro-anatomical modeling, biomolecular modeling	503,412	4,765,531
5 P41 RR 00757-10	Joseph Kraut, Ph.D. Univ. of California La Jolla, Ca.	Computer Resource for Biomolecular Research	Computer-based automated laboratory systems	Biomolecular modeling, on-line acquisition of x-ray crystallographic data	290,851	2,457,282
5 P41 RR 00898-09	Frederick Brooks, Ph.D. Univ. of North Carolina Chapel Hill, N.C.	Graphics Resource for Molecular Studies	Interactive computer graphics	Biomolecular modeling of proteins and nucleic acids	280,139	1,911,857
5 P41 RR 01081-05	Robert Langridge, Ph.D. Univ. of California San Francisco, Calif.	Special Research Resources for Biomolecular Graphics	Stand alone medium computer and graphics	Biomolecular modeling	401,028	2,715,607

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Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
I. Knowledge Engineering and Information Technology in Biomedicine						
B. Information Technology (continued)						
5 R23 RR 01372-02	Hoang Kim Tuy, Ph.D. Univ. of Pennsylvania Philadelphia, Pa.	3-D Reconstruction of Organs from Limited Range of Views		Mathematical studies relating to image analysis in biology	57,526	113,275
1 R13 RR 01628-01	Walter B. Goad, Ph.D. Aspen Center for Physics Aspen, Col.	Workshop on Computational Analysis of DNA Sequences		Workshop developing approaches to solve the computational needs of molecular biologists	19,830 (Co-funded-Total $22,830)	--

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Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
II. Biomedical Engineering and Digital Technology						
A. Biomedical Engineering						
5 P41 RR 00857-08	Wen H. Ko, Ph.D. Case Western Reserve Univ. Cleveland, Oh.	Biomedical Electronics Resource	Microelectronics fabrication, packaging and evaluation	Micro-electrodes, solid state physical and gaseous sensors, implant telemetry	815,553	4,742,856
5 P41 RR 01086-06	James B. Angell, Sc.D. Stanford Univ. Stanford, Ca.	Resource for Silicon Biomedical Transducers	Microelectronics and micromaching of sensors	Biomedical transducers for clinical research	278,610	1,705,191
1 R24 RR 01362-01	Lewis J. Thomas, Jr., M.D. Washington Univ. St. Louis, Mo.	Tissue Characterization Via Ultrasonic Imaging	Digital characterization and image reconstruction	Characterization of acoustic properties of biological significance	282,995	--
B. Digital Technology						
5 P41 RR 00374-16	Theodore H. Kehl, Ph.D. Univ. of Washington Seattle, Wash.	Support for Physiology and Biophysics Computer	BASIL computer system	Computer support to on-line control and analysis of physiology and biophysics	408,721	3,287,762
3 P41 RR 00396-14S2 3 P41 RR 00396-14S3 3 P41 RR 00396-14S4	Jerome R. Cox, Jr., Sc.D. Washington Univ. St. Louis, Mo.	A Resource for Biomedical Computing	Dedicated computers and macromodule systems	Information system technology cardiac rhythm monitoring, biomolecular modeling, positron-emission tomography	45,628 268,905 88,818	23,578,549

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Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
			II. Biomedical Engineering and Digital Technology			
B. Digital Technology (continued)						
3 P41 RR 01089-05S1 5 P41 RR 01089-06	Robert Schoenfeld, D.E.E. Rockefeller Univ. New York, N.Y.	A Microprocessor Biotechnology Resource	Application of microprocessor-based instruments to biology	Development of microprocessor-based systems for biological research	654 300,763	1,232,259
1 R13 RR 01358-01	Lewis J. Thomas, Jr., M.D. Washington Univ. St. Louis, Mo.	Workshop on Time of Flight Emission Tomography		This workshop brought together scientists from several countries to discuss PET scanners incorporating time of flight information	10,400 (Co-funded-Total $15,250)	--
1 R24 RR 01379-01	Charles E. Molnar, Sc.D. Washington Univ. St. Louis, Mo.	Research in VLSI Systems for Biomedical Applications	Development of methods of incorporating biomedical software capabilities in silicon	Solid state electronics and digital systems for biomedical research	783,063	--
1 P41 RR 01380-01	Lewis J. Thomas, Jr., M.D. Washington Univ. St. Louis, Mo.	A Resource for Biomedical Computing	Dedicated hardware and software systems tailored to biomedical needs	Enhanced PET scanning systems using time of flight data, image processing systems for analysis of radioautographs, system for early recognition of visual defects in glaucoma	526,140	--

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Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
A. Biomolecular Structure and Function						
1. Mass Spectrometry						
5 P41 RR 00317-16	Klaus Biemann, Ph.D. M.I.T. Cambridge, Mass.	Mass Spectrometry Facility for Biomedical Research	High resolution, MS, GC/medium resolution MS	Drug identification, drug metabolism, molecular structure analysis	400,915	4,149,793
5 P41 RR 00480-14	Jack T. Watson, Ph.D. Michigan State Univ. East Lansing, Mich.	Mass Spectrometry Facility	High resolution MS, GC/MS, field desorption MS	Metabolites in biological fluids, structure, determination of lipids, analysis of complex mixtures	178,729	1,821,319
5 P41 RR 00862-09	Frank H. Field, Ph.D. Rockefeller Univ. New York, N.Y.	A Mass Spectrometric Biotechnology Resource	Low and High resolution MS, GC/chemical ionization quadrapole MS	Fission fragment MS, drug metabolism, drug essays, peptide sequencing	237,419	1,350,587
5 P41 RR 00954-06	William F. Holmes, Ph.D. Washington Univ. St. Louis, Mo.	A Resource for Biomedical Mass Spectrometry	GC/medium resolution MS; chemical ionization	Drug and vitamin metabolism; inborn metabolic errors	225,598	1,651,239
5 P41 RR 01152-02	Paul V. Fennessey Univ. of Colorado Denver, Col.	Clinical Mass Spectrometry Resource	GC/medium resolution MS	Pharmacology and clinical medicine	103,496	443,765

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Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
A. Biomolecular Structure and Function (continued)						
1. Mass Spectrometry (continued)						
7 P41 RR 01614-01 (previously #00719)	A.L. Burlingame, Ph.D. Univ. of California San Francisco, Calif. (previously at Berkeley, Calif.)	Bio-Organic, Biomedical Mass Spectrometry Resource	High resolution mass spectrometry	Chemical structure identification, MS on mixtures, high mass carbohydrates	599,151	3,364,542
2. Nuclear Magnetic Resonance						
5 P41 RR 00292-17	Aksel A. Bothner-By, Ph.D. Mellon-Pittsburgh Carnegie Corporation Pittsburgh, Pa.	NMR Facility for Biomedical Studies	600 MHz NMR spectrometer	Structure and function of hemoglobins, biological membranes, proteins	309,519	2,645,524
5 P41 RR 00542-12	George McDonald, Ph.D. Univ. of Pennsylvania Philadelphia, Pa.	Middle Atlantic NMR Facility	220 MHz, NMR spectrometer; 360 MHz, NMR spectrometer	Enzyme/substrate interaction mechanisms; RNA structure	192,568	2,015,911
5 P41 RR 00574-10	David M. Grant, Ph.D. Univ. of Utah Salt Lake City, Utah	Regional Research Facility in NMR	100 MHz NMR spectrometers; 300 MHz NMR spectrometer	^{13}C labelled macromolecules; ^{15}N-^{13}C coupling constants of depeptides	--	1,719,875
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Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
A. Biomolecular Structure and Function (continued)						
2. Nuclear Magnetic Resonance (continued)						
5 P41 RR 00711-10	Oleg Jardetzky, M.D. Stanford Univ. Stanford, Calif.	High Frequency NMR Biotechnology Resource	360 MHz NMR spectrometer	Conformational changes on the lac-repressor proteins, membrane immuno chemistry enzyme-substrate complexes	296,969	2,593,470
3 P41 RR 00995-06S1 5 P41 RR 00995-07	Leo J. Neuringer, Ph.D. M.I.T. Cambridge, Mass.	A National NMR Facility for Biomolecular Research	500 MHz NMR spectrometer; 290 MHz NMR spectrometer for studies of solids	Model membrane systems; lipid-protein interactions	3,172 203,958	1,401,023
5 P41 RR 01077-06	John H. Markley, Ph.D. Purdue Univ. West Lafayette, Ind.	A Regional NMR Resource for Biomolecular Research	500 MHz NMR spectrometer	Macromolecular structure studies	186,640	1,501,044
5 P41 RR 01317-02	George C. Levy, Ph.D. Syracuse Univ. Syracuse, N.Y.	NIH Resource for Multi-Nuclei NMR and Data Processing	360 MHz wide bore NMR spectrometer and computer data processing for NMR data	A regional laboratory for biological NMR studies	204,141	696,337

Biotechnology Resources Program
Division of Research Resources
Grants Funded During FY 1982

Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
A. Biomolecular Structure and Function (continued)						
2. Nuclear Magnetic Resonance (continued)						
1 R13 RR 01329-01	Martin C. Moore-Ede, Ph.D. Harvard Medical School Boston, Mass.	Symposium on Mathematical Modeling of Circadian Systems		This workshop dealt with advanced methodology and applications in modeling periodic behavior of testing systems	--	7,845
1 R13 RR 01611-01	Oleg Jardetzky, M.D. Stanford Univ. Stanford, Calif.	Conference on Magnetic Resonance		Magnetic resonance applications in biological areas	17,000 (Co-funded-Total $30,000)	--
3. Other						
5 P41 RR 00886-08	Edward L. Powers, Ph.D. Univ. of Texas Austin, Tx.	Center for Fast Kinetics Research	Electron pulse 5.5 MeV Van de Graff accelerator for radiolysis studies	Reactions of DNA and OH radicals; dose rate effects in irradiated cells	279,487	1,963,238
5 P41 RR 00962-07	Nicholas A. Matwiyoff, Ph.D. Univ. of California Los Alamos, N.M.	A National Stable-Isotopes Resource at Los Alamos	Provision of labelled compounds with stable isotopes of C, O, and N for biological research	Syntheses of labelled compounds with stable isotopes	331,228	1,633,148

Biotechnology Resources Program
Division of Research Resources
Grants Funded During FY 1982

Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
A. Biomolecular Structure and Function (continued)						
3. Other (continued)						
2 P41 RR 01008-07	James S. Hyde, Ph.D. Medical College of Wisconsin Milwaukee, Wis.	National Biomedical ESR Center	ENDOR, ELDOR pulse ESR spectrometers	Clinical applications of ESR, structure of free radicals in biological materials, enzyme kinetics; paramagnetic changes during tumor development	266,034	1,686,121
5 P41 RR 01135-05	Robert M. Kretsinger, Ph.D. Univ. of Virginia Charlottesville, Va.	Development of an Area X-Ray Diffractometer	A multiwire detector provides the basis for rapid x-ray data collection	Emphasis will be on data collection for protein crystals	193,127	927,507
5 P41 RR 01209-03 3 P41 RR 01209-03S1	Arthur I. Bienenstock, Ph.D. Stanford Univ. Stanford, Calif.	A Synchrotron Radiation Biotechnology Resource	Extended x-ray absorption, fine structure spectroscopy flourescence spectroscopy, x-ray diffraction	Structure of metal containing proteins	306,276 196,838	1,759,128

Biotechnology Resources Program

Division of Research Resources

Grants Funded During FY 1982

Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
A. Biomolecular Structure and Function (continued)						
3. Other (continued)						
1 P41 RR 01237-01A1	Richard M. Lemmon, Ph.D. Univ. of California Berkeley, Calif.	A National Tritium Labeling Facility	Labeled compounds of very high activity can be prepared	Novel labeling methods for biological compounds	466,018	--
1 P41 RR 01348-01	Robin M. Hochstrasser, Ph.D. Univ. of Pennsylvania Philadelphia, Pa.	Ultrafast Optical Processes Laboratory	Picosecond measurements of fluorescence and Raman spectra	Use of picosecond laser optical techniques to study biological processes	445,970	--
1 P41 RR 01633-01	Britton Chance, Ph.D. Univ. City Science Center Philadelphia, Pa.	Metalloenzymes, Proteins and Models (Research Resource)	Use of synchrotron radiation to study biological molecules	Emphasis is on EXAFS and diffraction studies of metalloenzymes and proteins	427,071	--
3 R01 GM 08710-21S1	Margaret O. Dayhoff, Ph.D. Georgetown Univ. Medical Center Washington, D.C.	Computer Study of Sequences of Amino Acids in Proteins	Computerized nucleic acid and protein sequence data bases	Developing nucleic acid and protein sequence data bases	--	25,000

Biotechnology Resources Program
Division of Research Resources
Grants Funded During FY 1982
Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
A. Biomolecular Structure and Function (continued)						
3. Other (continued)						
1 R13 GM 30505-01	Wayne A. Hendrickson, Ph.D. Gordon Research Conferences Kingston, R.I.	Gordon Conference on Diffraction Methods in Molecular Biology		Diffraction methods	3,000 (Co-funded-Total $10,910)	--
B. Cellular Structure and Function						
1. Electron Microscopy						
5 P41 RR 00570-12	Hans Ris, Ph.D. Univ. of Wisconsin Madison, Wis.	Electron Microscope Facility for Biomedical Research	1 MeV electron microscope	3-D structure of chromosomes neuronal tissues, frozen tissues	279,164	2,286,031
5 P41 RR 00592-13	Keith R. Porter, Ph.D. Univ. of Colorado Boulder, Col.	High-Voltage Electron Microscopy of Biological Systems	1 MeV electron microscope	3-D structure of whole-cultured cells, intracellular systems, isolated mitotic apparatus	358,795	4,396,030
2 P41 RR 00715-10	Joseph S. Wall, Ph.D. Associated Universities Upton, N.Y.	Electron Microscope Facility	50 KV scanning transmission electron microscope	Viruses, nucleic acids, membranes	353,840	2,179,051

Biotechnology Resources Program
Division of Research Resources
Grants Funded During FY 1982
Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
B. Cellular Structure and Function (continued)						
1. Electron Microscopy (continued)						
5 P41 RR 01214-03	Michael Beer, Ph.D. Johns Hopkins Univ. Baltimore, Md.	Atomic Microscopy of Labeled Systems: A STEM Facility	40 KV scanning transmission electron microscope	Localization of heavy atom stains on proteins, nucleic acids and cells	238,171	813,938
5 P41 RR 01219-02	Donald F. Parsons, Ph.D. New York State Department of Health Albany, N.Y.	High Voltage EM Biological Facility for the Northeast	1 MeV electron microscope	Provides user services and collaboration on cell biology studies using high voltage electron microscopy	103,097	223,773
1 R13 RR 01314-01	Lee D. Peachey, Ph.D. Trustees of the Univ. of Pennsylvania Philadelphia, Pa.	Biomedical High Voltage Electron Microscopy Conference		A review of progress and recent advances in high voltage electron microscopy	--	7,845
2. Other						
3 P41 RR 00679-10S1 2 P41 RR 00679-11	Claude P. Lechene, M.D. Harvard Medical School Boston, Mass.	National Biotechnology Resource in Electron Probe Microanalysis	CAMECA electron microanalyzer	Elemental composition of biological tissues	16,855 556,682	3,992,203

Biotechnology Resources Program
Division of Research Resources
Grants Funded During FY 1982
Table III

Grant Number	Principal Investigator and Institution	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
III. Technologies for Study of Biomolecular and Cellular Structures and Function						
B. Cellular Structure and Function (continued)						
2. Other (continued)						
5 P41 RR 01192-03 3 P41 RR 01192-02S1	Michael Berns, Ph.D. Univ. of California, Irvine Irvine, Calif.	A Laser Microbeam Biotechnology Resource	Micro-focused laser systems	Microsurgery on cells and tissues	137,365 726	808,396
1 P41 RR 01315-01A1	L. Scott Cram, Ph.D. The Regents of the University of California Los Alamos, N.M.	National Flow Cytometry and Sorting Research Resource	Cell sorting and flow cytometry	Chromosome high resolution image sorting multiwavelength cell sorting	682,553	--
1 P41 RR 01395-01	Lionel F. Jaffe, Ph.D. Marine Biological Laboratory Woods Hole, Mass.	Proposed National Vibrating Probe Facility	Determinaton on current flow patterns surrounding cells using a mutating electrode	Electrical current patterns viz-a-viz cellular dynamics	324,394	--
1 R13 CA 33891-01	Alexander R. Margulis, M.D. Univ. of California San Francisco, Calif.	1st Annual Conference Magnetic Resonance Imaging Society		NMR imaging	3,500 (Co-funded-Total $30,750)	--

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Biotechnology Resources Program
Division of Research Resources
Contracts Funded During FY 1982

Table III

Contract Number	Name and Address of Contractor	Title	Capability	Research Emphasis or Applications	FY 1982 $ (Total Costs)	Cumulative $
NOI RR 9 2107	ADP Network Services, Inc. Waltham, Mass.	Hardware Maintenance Contract in Support of PROPHET System	PROPHET time-sharing computer resource	Chemical/biological information handling	--	2,335,968
NOI RR 8 2118	Bolt Beranek and Newman, Inc. Cambridge, Mass.	Software Development Maintenance and Technical Assistance for PROPHET System	PROPHET time-sharing computer resource	Chemical/biological information handling	2,327,340 (excludes intramural funds at $616,032 and interagency transfers at $107,500)	10,870,106

October 1982

Fiscal Year 1982
Annual Report
General Clinical Research Centers Program Branch
Division of Research Resources

PROGRAM DESCRIPTION

Background

As biomedical scientists try to understand and cope with the complexities and basic biological problems of human disease processes, they must at some point study man himself. Although various animal and *in vitro* models can stimulate some human biological systems and disorders, they cannot substitute for a direct study of the intact human organism and its disease states. Perceiving the need for increased patient-oriented research, the United States Senate in 1959 urged special studies on humans, leading to the establishment of the first General Clinical Research Centers (GCRCs).

The GCRC Program makes available to scientists the resources necessary for the conduct of high quality clinical research. Successful clinical research depends as much on the research setting as on the research protocol itself. The Centers are intended to provide as optimal an environment as possible, including all the personnel and technical tools which researchers need to provide superior care for research patients while acquiring new health knowledge.

The research capacity of the entire GCRC Program (74 different Centers) is equivalent to that of a single 600-bed hospital devoted entirely to human studies. The Center can accommodate both outpatients and inpatients. The Program provides for the specialized care needed for studies on both adults and children; currently 88 of the nearly 600 beds are on pediatric wards or in children's hospitals. Sixty-six of the 74 Centers admit pediatric patients on a regular basis. In addition, one Center is devoted to research on maternal and fetal problems surrounding delivery, and another is for research involving premature infants.

The Program provides a service to investigators supported by NIH and other sources which enables them to study human biology with the latest laboratory techniques. Since its inception, the Program has supported the entire cost of the Centers, except that Centers are reimbursed for routine care and treatment of one-third of the research patients on the Centers by third party carriers at the normal rates.

Mission

The Centers provide as optimal a clinical research environment as is possible, including all the latest supporting systems and technical tools which researchers need to acquire new health knowledge.

Objectives

In pursuing its mission, the GCRC Program has the following specific objectives:

- to learn more about normal and abnormal body function, and about the cause, progression, prevention, control, and cure of human disease;
- to provide an optimal setting for controlled investigation by clinical scientists supported through the NIH and other organizations;
- to encourage increased collaboration between investigators in the basic and clinical sciences;
- to encourage, develop, and maintain a national corps of expert clinical investigators;
- to provide a resource where advances in basic scientific knowledge may be translated into methods for improved patient care.

Program Operations

A "typical" Clinical Research Center supports one or two medical program directors, as well as 12 nurses, three dietitians, two laboratory technicians, and some administrative personnel. The unit can accommodate both outpatients and inpatients. The budget of a typical research center is shown on Table 1.

Most Clinical Research Centers contain approximately eight beds; the range is four to thirty. Other subunits of a Center are treatment rooms, a core laboratory, a diet kitchen, patients' lounge space, a nurses' station, a conference room, and outpatient space. The number of patient days, outpatient visits, and centers is shown in Table 2. The program budget in real and constant dollars is shown in Figure 1.

The GCRC Program pays the hospital costs of all patients admitted to the Centers solely for research purposes. About 35 percent of the patients participating in research projects require hospitalization for diagnosis or treatment, and these patients are billed for this part of their stay, usually through third-party insurers.

The core laboratory and metabolic kitchen are two parts of a Center essential to maintaining its controlled environment. They provide tests or services not readily available elsewhere in the hospital. When routine tests are required, the hospital's clinical laboratory often handles them, freeing the core laboratory for more specialized work. However, standard hospital laboratories are not always able to provide routine tests and assays with the degree of speed or accuracy needed by clinical investigators, either because of heavy workloads or a lack of special equipment; these must be provided by the core

laboratory. The kinds of tests performed by core laboratories vary from Center to Center, depending on the requirements for core services. Consequently, the equipment and procedures vary from one laboratory to another.

One of the most important elements of the Center is the group of highly trained paramedical personnel. Nurses, dietitians, laboratory workers, and other support personnel, trained in the methodology of clinical research, perform duties essential to maintaining high clinical research standards.

CLINFO

The CLINFO System is a computer-based data management system designed for clinical investigators. The prototype version was tested by clinical investigators in 1977 and found to be useful for managing and rapidly analyzing their data. Subsequently, the GCRC Program Branch has awarded fourteen production versions of CLINFO to the GCRCs, as shown in Table 3. This expanded clinical investigator community has accepted the CLINFO System with some enthusiasm, and several additional GCRCs are applying for the system. Bolt, Beranek, and Newman, Inc., the production version purveyor, has sold and installed three CLINFO systems in non-GCRC sites and has sold three additional systems.

The GCRC Program Branch is collecting more specific evaluation data on the extant CLINFO Systems through Annual Reports that the Centers submit to the GCRC Branch. The twelve CLINFO sites reporting this past year have used a total of 36,000 connect hours, with the more mature systems exceeding 6,000 connect hours each. CLINFO has been used in the preparation of 317 GCRC publications and 211 abstracts in the past year. The present cost to the GCRC Program for the eighteen awarded CLINFO Systems is $1,421,000. The incremental costs to the Program from 1978 on can be noted in Table 4.

The system managers continue to be an integral part of the CLINFO System. The second meeting of the Organization of the CLINFO System Managers (OCSM) was held at Johns Hopkins University School of Medicine on October 29-31, 1981. The organization's charter provides data for management assistance to investigators and to the maintenance and enhancement of the CLINFO Centers in a manner designed to increase medical knowledge. The CLINFO utilization report form was developed and has been used for the CLINFO Annual Reports now submitted to the GCRC Branch. The next meeting of the OCSM is planned for October, 1982. The possibility of initiating user fees for CLINFO will be an agenda item for the upcoming meeting.

During Fiscal Year 1982, new guidelines for an application for a CLINFO system were developed, and a final draft was sent to all GCRCs. One section which received particular attention was the characteriza- tion of the qualifications of the system manager. The system manager will no longer be reviewed by the GCRC Committee and NARRC prior to approval of the application; instead, the system manager will be

selected by the institution according to the new guidelines and reviewed by Program staff prior to assuming the post.

CLINICAL ASSOCIATE PHYSICIAN PROGRAM

The GCRC Program is extraordinarily interactive with the NIH grant and contract programs for clinical research as a whole. The program is sensitive to changes in clinical research directions and utlimately depends on the flow of awarded dollars to competent clinical investigators in academic medical centers with GCRCs. Thus the program depends on an adequate supply of well-trained investigators interested and dedicated to clinical research. The recent precipitous decline in the number of young physicians entering biomedical research careers, 1/ during the mid-1970s, was one such change that prompted the GCRCP to initiate the Clinical Associate Physician (CAP) Program. This program, designed to encourage young physicians to enter careers in clinical investigations, has since produced 85 graduates of whom approximately 90% have remained in academic medicine. To date, half of these graduates in academic medicine have obtained NIH support for their clinical research investigations.

PROGRAM ACCOMPLISHMENTS

The GCRC Program has been in operation for 20 years, but the Program has lacked a comprehensive review of its scientific contributions. Thus, the GCRC Program decided to evaluate the major scientific contributions from the Centers since the program was initiated. The project has been divided into two phases.

The first phase of this evaluation was directed at obtaining lists of significant publications from the GCRCs. With advice and guidance from the GCRC Committee and the extant GCRCs, areas of clinical medicine were identified in which major advances have taken place in the past 20 years. A list of 31 categories and over 200 subcategories was developed from this effort. Center program directors were given this list and asked to identify those articles which they thought were most significant, according to a suggested list of criteria. This exercise resulted in the submission to the GCRC Branch of over 7,000 articles from 77 GCRCs.

The second phase is to be a continuing process of evaluating this group of articles and developing reports on selected topics. For this purpose, workshops have been held and expert consultants have been asked for evaluations. The first four topics selected were Neuroscience, Diabetes, Neonatologyy and Related Immunology, and Hypertension. A GCRC Committee member chaired a workshop of consultants on each topic. The consultants presented special subtopic reports to the chairperson, who compiled and edited the subtopic sections. The report on Diabetes has been completed and distributed. The report on Neuroscience is almost complete and a summary has been published in the Research Resources Reporter. The remaining two reports are scheduled for completion in 1982.

1/ Clinical Research Manpower Report of the Ad Hoc Committee on Clinical Research Training. AAMC, One Dupont Circle, N.W., Wash., D.C., February, 1980

FUTURE PROGRAM DIRECTIONS

Needs and Opportunities

Clinical research may be defined as research on patients, carried out as part of studies on the causes, mechanisms, diagnosis, treatment, prevention, and control of disease. Increased effort is needed to sustain the national level of high quality activity in this area, because of disturbing declines observed in clinical research activities, in the number of new investigators entering clinical research, and in support for facilities for this purpose.

Clinical investigations can take many forms, but most often the critical link between basic science and patient care can only be achieved by systematic observation of individual patients in a controlled environment like that of a GCRC. Most inpatient research on conditions such as coronary disease and other cardiac disorders, hypertension, kidney disease, and diabetes, and much of that on cancer, is carried out in these Centers. Investigators holding NIH research project grants or working on NIH Center grants usually have adequate provisions for laboratory support for their human studies, but do not have funding for the patient bed and clinical care costs. The expenses for such studies cannot be borne by the subjects of the investigations or by hospitals or insurance carriers. As a result, an investigator without access to facilities like those on GCRCs often cannot address the clinical application of findings from laboratory studies.

The GCRC Program funds 75% of the extramural research inpatient care for research supported by the NIH categorical institutes. More than 3000 projects are conducted at the Centers, by more than 3000 investigators. The extent to which the Centers expand the application of NIH-funded research to direct studies on human disease problems is illustrated by analysis of NIH support of GCRC-based investigators. Investigators utilizing the Clinical Research Centers in 1981 received over $400 million in support from other PHS grants and contracts, representing a large proportion of NIH activity impacting on extramural research subjects, as shown in Table 5. Few of these investigators have hospitalization or patient care costs included in their NIH awards. It is clear that the GCRCs provide the major means for carrying out the crucial human applications of these studies, in which insights reached in basic research are translated to clinical situations. These Centers are thus a most important national resource for advances in patient care. Maintenance of the Centers' function is essential for efforts to improve the health of the American people and to apply the knowledge gained in basic research to the prevention, control, and amelioration of human illnesses. Manpower maintenance programs can be efficiently developed in these Centers so that a skilled corps of clinical investigators can continue to work toward improving the well-being of the American people.

As resources permit, the program staff will be exploring the following specific areas of need:

1. An opportunity exists to enlarge the base of GCRCs located in key medical institutions across the country. While medical schools increased in number from 100 to 125 during 1968-1981, the number of GCRCs has declined from 91 to 74. Over a five-year period the base should be increased by 15 to 20 percent.

   Applications for GCRCs from dental schools and research hospitals have also recently increased the need to expand the base of Centers. The total base of eligible institutions, including those now in the program and those with potential to create GCRCs, is estimated at over 100 institutions, and some large research institutions can support more than one productive GCRC (e.g., separate adult and pediatric centers).

   Another area of need has been identified in minority medical schools. During the past two years the program has worked with the Minority Biomedical Research Program to expand the opportunities for clinical research in minority medical schools. The program plans call for continued monitoring of this development.

2. Rapid growth of outpatient activities in the Center's program and requests for development of new outpatient facilities at other Centers indicate a need for expansion of the base of outpatient units. Outpatient resources are particularly useful for studies in clinical pharmacology and chronic metabolic conditions, and provide for a considerable increase in the number of research patients who can be investigated.

3. Although a few institutions now have CLINFO, a computer-based system for management and analysis of clinical research data, high demands for greater distribution of this system to a larger sphere of institutions continues. This system is well received by clinicians, as it allows interrogation and analysis of research data bases in ways that greatly assist the creation of scientific hypotheses and interpretation of data. Development and distribution of the software and hardware ensembles of CLINFO technology could be substantially beneficial to the GCRC Program's productivity if placed in at least two-thirds of the Centers.

   As part of its continuing effort to provide data management facilities for clinical investigation in the GCRC Program, additional systems will be considered for development as clinical research resources. One such system is the PROPHET

System, a national time-shared computer network which was developed and managed by the Biotechnology Resources Program (BRP), DRR. This network offers a comprehensive set of tools for table making, statistical analysis, graphing, curve fitting, and mathematical and molecular modeling. Stimulated by discussions of various groups within DRR, the GCRC Branch and the BRP Branch initiated negotiations about implementing a trial of the PROPHET System on GCRCs to evaluate further its usefulness in analyzing data obtained in clinical investigation. Staff members of both branches are developing a request for application (RFA) inviting GCRCs to apply for a PROPHET System. Plans are to consider placing PROPHET terminals in two GCRCs during the next fiscal year.

4. More innovative technologies should be introduced into core laboratory facilities. Centers have recently encountered difficulties in learning about and gaining access to the most recent advanced technology applicable to clinical research. Some of the technology is very expensive and requires technical skills not usually acquired in the training and experience of physicians. High pressure liquid chromatography (HPLC) is one well-developed technology that is now becoming widely applicable to clinical investigations, but which because of cost and other factors is not readily available to most investigators. It is appropriate for a core laboratory resource because of its breadth of applicability to metabolic studies of proteins, fats, steroids, drugs, hormones, and metabolic intermediates. It provides advantages of high specificity and short lag time, relatively low operational expense, and absence of radioactive waste disposal problems.

5. The GCRC Program evaluated the feasibility of engaging in several new technologies which could be important for clinical research. For efficient review of these technologies, a subcommittee was formed consisting of several members of the GCRC Advisory Committee, with the collaboration of the Branch Chiefs of the GCRC Program and the Biotechnology Resources Program and some of their staff members.

   One area which seems to be of great interest to the clinical investigator is the use of stable isotope labeled compounds analyzed by mass spectroscopy. The committee agreed to pursue this area in close cooperation between the GCRC and the BRP.

   Another area which may be important to clinical research, which might need support, is neuropeptide analysis.

6. There is a need to enhance the management of small scale clinical trials, which in the forms of experimental therapeutics may consist of as much as forty percent of the research activity on GCRCs. Small trials, in contrast to large ones, often have inadequate staff support, which

interferes with effective data collection and management. This makes a lack of continuity and consistency in carrying out tasks. A recently completed survey supported by an evaluation contract to characterize clinical trials and to determine the appropriate and needed resources to improve the clinical trial capabilities of GCRCs is undergoing further analysis to determine the best ways to improve clinical trial capabilities of the GCRCs.

7. GCRCs constitute an exceptionally favorable environment for developing clinical research investigators and sustaining their continued pursuit of research careers, since they provide a complete, well-regulated research and care system for direct studies with patients. GCRCs can play an important role in helping to meet the national need for well-trained medical researchers. Bringing additional young investigators into the research enterprise is part of this role. Retaining already established and highly skilled researchers is another. Many difficulties and disincentives are in the path of medically trained personnel seeking long-term careers in clinical research.

   The GCRC Program staff and its advisors believe that competitive grant programs which provide reasonable and stable salaries for those interested in clinical investigation will make this activity more attractive to talented physicians. In 1974, the Program initiated the CAP Program, which has been highly successful in attracting capable young investigators into academic positions in clinical research. It now seems opportune to provide incentives to induce physicians established in research careers to continue in patient-oriented investigations. The target group would be those who are accomplished, successful, peer-reviewed scientists. Often these people are forced by the time demands of teaching and patient care to concentrate their research efforts on work which can be scheduled flexibly, such as studies on small mammals or on cell-free systems. A program is needed which would provide an incentive to capable clinical scientists to concentrate their efforts on patient-related studies.

Program Directors' Conference

A conference of Clinical Research Center Program Directors is planned for December 1982. The meeting is to be a joint project of the Clinical Research Center Program Directors Organization and the GCRC Branch. The major topics, to be addressed in workshop format, are Industry-Related Research, Collaborative and Cooperative Efforts Among Centers, Promotion of Clinical Investigation, New Technologies for Clinical Research, Organization and Operation of Research Centers, and Diversification of GCRC Utilization.

The Program Staff believes that in-depth discussions of these issues will help define the special problems, needs, and goals that apply to human investigation in U.S. Medical Centers. This should lead to a more efficient operation of existing Centers and contribute to the growth and development of the program during the next decade.

PROGRAM HIGHLIGHTS

Each year the projects on the Centers shed new light on a number of the perplexing disease problems which are subjected to study. Examples of these highlights follow:

PATHOGENESIS

Thyroid Cancer

New evidence indicates that some cancer cells change biochemically as they develop, and that these changes correlate with increasing virulence of the cancer and worsening of the prognosis. Initially, the cells are homogeneous, or at least very similar, becoming more heterogeneous as the disease progresses. The first practical application of this finding has come in the counseling of some patients with an inherited tendency to develop medullary thyroid carcinoma. Homogeneous tumors are much less likely to spread widely and aggressively than those with a mixture of cells with extreme biochemical differences.

Reye's Syndrome

Six children in four unrelated families developed during fasting a severe illness characterized by hypoglycemia, coma, and other features reminiscent of Reye's syndrome. The condition was due to a defect in the children's ability to oxidize fatty acids, and was associated with very low levels of carnitine, a co-factor for this process. The discovery of this disorder raises the possibility that in some patients Reye's syndrome is due to an inherited disorder of fatty acid metabolism.

A similar disorder mimicking Reye's syndrome is caused by a defect in the biosynthesis of carnitine itself. A dramatic improvement in this condition has been obtained in a single patient treated with carnitine therapy coupled to a low fat diet.

Mercury Poisoning

It has been suspected that mercury exposure represents a health hazard of dental practice, but no analysis of the effects of chronic exposure has been made. In a recent study it was found that dentists with high mercury levels have a 30% incidence of polyneuropathies, while dentists

without detectable mercury levels have a zero incidence. Other health complaints are also greater. Apparently the use of mercury as a restorative material can result in a long-term health risk to dentists.

Diabetes

Normal parents of diabetic children sometimes have blood vessel changes like those commonly found in adults with diabetes. When these changes are present, the gene for human leukocyte antigen DR4 usually can be found as well. This does not mean that any one gene causes diabetes, but it suggests that a gene involved in diabetes is on the short arm of the sixth chromosome, linked to the DR locus.

Pseudohermaphroditism

A rare defect in the metabolism of steroid hormones, preventing the conversion of testosterone to androsterone, causes certain genetically male children to be born with apparently female genitalia. Normal male genitalia develop at puberty. Though raised as girls, these individuals mostly develop normal male attitudes and normal sexual orientation after puberty. Social adjustment can be difficult, but it is often successful, refuting the widely-held idea that sexual identity is established at a very early age and can never be changed.

Sunburn

The biochemical substances involved in producing sunburn in response to ultraviolet light have been poorly understood. The sunburn reaction is important because it may bear on skin cancer and premature aging, two conditions associated with ultraviolet light exposure. Recent evidence that histamine, which dilates blood vessels, increases four-fold in the blood in response to sunburn, suggest that this substance may be the initial mediator of the sunburn reaction. Later elevations in prostaglandin E_2, a hormone released by most tissues of the body in response to injury, suggest that prostaglandins may mediate later phases of sunburn.

Functional Renal Failure

One of the most mysterious of the many causes of kidney failure is "functional renal failure", in which it appears that blood flow is shunted away from the kidney. Its most common and severe form occurs in patients with liver disease. Studies in animals suggested that the production by the kidney of thromboxane A-2, a very potent vasoconstrictor substance, may be involved in this disease. Studies in humans had to await the development of specific radioimmunoassays, worked out by GCRC investigators over a three-year period and validated by a very specific mass spectrometer method at the GCRC-supported 'CLINSPEC' facility. Studies utilizing these assays have produced the exciting finding that urinary thromboxane is dramatically increased in patients with this disorder, providing a clue to its etiology and a lead to its possible therapy with inhibitors of thromboxane action.

Asthma

It has been discovered that many asthmatics who believe they are allergic to certain foods may actually be sensitive to a type of chemical preservative. This preservative, called potassium metabisulfite, is used to preserve a wide variety of foods and beverages, from restaurant salads to wines. It has no effect on most people, but in others it may precipitate an asthma attack so severe that emergency treatment is required to restore breathing.

PREVENTION

Diabetes

The way fat is distributed on the human frame appears to indicate the degree of risk that people have of developing diabetes. Individuals whose fat is distributed mostly above the waist are more likely to develop diabetes than those who carry most of their excess weight in the hips and thighs. The bigger the waist compared to the hips and thighs, the higher the risk of developing diabetes. This pattern of upper-body obesity is a clear marker of increased diabetes risk which is easy to recognize and could be widely used to identify those patients who should be carefully watched for early signs of this disorder.

Aging

It is generally believed that glucose intolerance, a decrease in the body's ability to handle glucose, is an inevitable result of aging. During the past year, however, it has been demonstrated that this intolerance is markedly alleviated in non-obese, physically fit, active older subjects. Thus, it may actually result from environmental factors such as obesity and decreased activity, rather than from normal aging. Since glucose intolerance may increase the risk of atherosclerotic heart disease, the prevention of age-related glucose intolerance by proper nutrition and exercise may provide an effective way to reduce the frequency of heart attacks.

Immunodeficiency

A very high incidence of severe infections, especially recurrent pneumonias, occurs in Navajo infants. It has been found that these infections result from a high incidence of severe combined immunodeficiency in these children. Definition of this problem in the Navajo population has allowed for the early recognition of the children with this disorder, so that appropriate therapy can be initiated early, preventing possibly fatal infections.

DIAGNOSIS

Hypoglycemia

Fasting has been the most useful general test for the diagnosis of hypoglycemia (low blood sugar), but may require 36-48 hours. Administration of 2-deoxyglucose, a competitive inhibitor of glucose transport which rapidly stimulates the hypothalamic response to hypoglycemia, has been found to be as reliable as fasting in distinguishing hypoglycemic children, and it has the advantage of not producing symptoms associated with fasting.

Adrenal Tumors

Pheochromocytomas are tumors of adrenergic tissues which secrete hormones that cause severe symptoms, including hypertension. They are fatal if not excised. These tumors are not rare - at least 100,000 Americans suffer their effects - but they are often difficult to detect, even by sophisticated methods. A new radiopharmaceutical, metaiodobenzylguanidine, concentrates in pheochromocytomas, allowing their detection by a method called scintigraphy (mapping of the source of gamma rays emitted by a radioisotope).

Juvenile Diabetes

A number of patients with juvenile diabetes have been found to have limited joint mobility because of an abnormality of connective tissue. Subjects with this disability have more than three times the risk of microvascular complications from their diabetes than do those without it. Limitation of joint mobility thus identifies a population excessively at risk for the development of these complications.

Lead Poisoning

The use of heat guns by homeowners for do-it-yourself removal of old paint can result in volatilization of lead in the paint and excessive lead exposure. Physicians should be aware that lead poisoning can occur from avocational pursuits as well as vocational ones, and should maintain a high index of suspicion of the disease in patients presenting with nonspecific complaints referable to the central nervous and gastrointestinal systems.

Parathyroid Disorders

A new radioimmunoassay for parathyroid hormone in plasma has been developed by GCRC investigators. It is sensitive enough for measurements in normal human beings and specific for the biologically-active amino-terminal portion of the parathyroid hormone molecule. This new assay represents a technical advance which will be a major tool in studies of parathyroid function.

TREATMENT

Asthma

A method has been developed to desensitize persons who have asthma induced by aspirin. This method is important because aspirin is included in many drug preparations and cannot be easily avoided. Also, many aspirin-sensitive persons are also sensitive to other anti-inflammatory drugs, and some even to yellow food dye number 5; recent studies suggest that desensitization to aspirin may also desensitize patients to these other compounds.

Hydrocephalus

A technique has been developed for inserting a shunt into the brain of a fetus with incipient hydrocephalus, relieving excessive fluid pressure which could damage the brain. Ordinarily, hydrocephalic infants are treated by a shunt procedure performed after birth. In many instances, however, such severe brain damage has already occurred by the time of birth that the procedure only serves to facilitate custodial care. The new technique could allow many of these infants to develop more normally.

Difficult Labor

Between 1970 and 1978 the number of Cesarean sections nearly tripled, rising from 5 to 15% of all deliveries. A new analysis and recent research indicate that criteria for Cesarean section need not be as rigid as they have been, and that the number of sections can be reduced, especially when they are performed for dystocia (difficult labor) or because of a previous section. On one GCRC, a newly developed computer program allows diagnosis of the specific abnormality causing dystocia; this abnormality can then be treated specifically, often avoiding the requirement for a Cesarean section.

Heart Attacks

Ventricular fibrillation, a lethal complication of myocardial infarction, is characterized by rapid, irregular heartbeats that completely stop the pumping action of the heart. An automatic defibrillator that can be implanted in patients who are at high risk of developing ventricular fibrillation was successfully tested last year. Now a way to implant the defibrillator without major chest surgery has been devised, allowing the patient to leave the hospital in one week rather than two or three. The cost of the implantation method is half that of conventional surgery, and it frees the patients from the risk of complications of major chest surgery, such as severe pain or partial lung collapse.

Kwashiorkor

Researchers at a General Clinical Research Center have rehabilitated 12 of 14 victims of kwashiorkor, a severe illness caused by protein malnutrition, which typically has a 50 percent mortality. Kwashiorkor

occurs most commonly among poverty-stricken children in underdeveloped countries. Success of the therapy is attributed to prompt diagnosis and treatment of complications that frequently develop during nutritional rehabilitation.

Pituitary Tumors

Traditional therapy for patients with hormone-secreting pituitary tumors has been surgery or radiation therapy. In most cases the therapy has been empiric, based upon the preference of the physician. In an effort to predict patients' subsequent response to therapy, a large number of tests of pituitary function were conducted on a large number of patients with hyperfunctioning pituitary tumors. The results indicate that tumors secreting ACTH or growth hormone are best treated by surgery, while those secreting prolactin are not. This means that the choice between surgical and radiation therapies can be made by determining the secretory properties of the tumor.

Reproductive Disorders

Luteinizing hormone (LH), one of the gonadotropic hormones which control the functions of the gonads, is secreted from the pituitary gland in pulses which have an optimum frequency. If attempts are made to exceed this frequency by too-frequent injections of LH-releasing hormone, the pituitary becomes refractory and eventually completely unresponsive. This unexpected discovery has been exploited to develop remarkably effective new treatments for precocious sexual development in children and for infertility in men and women with subtle hypothalamic disorders.

Epidermidolysis Bullosa

Phenytoin, a drug widely used in the treatment of epilepsy, markedly reduces the lesions of a severe and often fatal disease of the skin and mucous membranes. Seventeen children with recessive dystrophic epidermolysis bullosa, a genetic disorder characterized by severe generalized blistering after minor wounds or even brief frictional trauma, were found to respond to oral phenytoin with a 52 percent decrease in blistering. No serious adverse effects of phenytoin were observed. Phenytoin thus represents a therapeutic option of relatively low risk in a disease for which there has been no rational therapy.

Heart Irregularities

A new anti-arrhythmic drug, encainide, has proved much more effective than previous treatments in suppressing a type of heart irregularity called ventricular ectopic depolarization. The drug has largely been ignored in clinical investigation because its half-life is short (3 hours), but investigators have now found that the therapeutic index of the drug is so high (i.e., it is so non-toxic) that it can be safely given in large doses every 8-12 hours.

Gastrointestinal Tumors

Instruments have been developed which allow bursts of laser energy to be applied through fiberoptic endoscopes used for examining the esophagus, stomach, duodenum, and colon. These bursts can be used to produce coagulation of bleeding vessels in an ulcer or small vascular tumors, or to destroy polyps (small nodules of the colon with the potential of becoming malignant). The laser treatment can replace abdominal surgery previously required for these conditions.

Ischemia

A method of intravenous injection of reserpine has been used to treat a type of severe hand or foot ischemia (lack of blood flow) caused by blood vessel spasm. The method allows prolonged contact of the drug with sympathetic nerve endings, blocking their action for up to five days. The procedure, which can be performed in an office or outpatient clinic, produces relief of symptoms for one to two weeks.

Congenital Heart Disease

Propanolol is a drug commonly used to alleviate symptoms in children with cyanotic congenital heart disease ("blue babies") until corrective surgery can be performed on them. With the low doses of drug recommended for children, however, therapeutic failures are common. It has now been found that larger doses, similar to those recommended for adults, can safely and effectively be used in children, producing a better response rate.

Fungal Meningitis

The yeast Cryptococcus neoformans is the most common cause of fungal meningitis. The disease is increasing in frequency because it tends to occur in patients whose immune mechanisms are compromised, such as transplant recipients and patients receiving cancer chemotherapy. Even though the untreated meningitis is fatal, a modification of treatment of its chronic forms has been developed that allows for patients to be treated as outpatients after the first two weeks of therapy. This results in a lowering of the average hospital cost to them from $12,000 to $7,000.

Cholestasis

Many children who have cholestasis (abnormal bile flow) since infancy develop chronic vitamin E deficiency. This is manifest as a slowly progressive central nervous system disease with poor coordination, rapid eye movements, and decreased sensation. Since vitamin E is not absorbed from the intestinal tract by these children, they must receive it by injection; this results in improvement in their neurologic disease, without obvious adverse effects.

Diabetes

Rapid progress has been made in recent years in the treatment of diabetes, using programmable pumps which automatically inject insulin subcutaneously. One new development in this field is the invention of a miniaturized, implantable pump about the size of a cardiac pacemaker; this can replace the bulkier, externally worn pumps now in common use. Another development is the technique of intraperitoneal infusion, which avoids the problems of intravenous lines and the uncertainties of subcutaneous infusions.

Kidney Dialysis

The hormone prostacyclin has been found to be a safe alternative to heparin in preventing blood clotting in patients being dialyzed on an artificial kidney. Moreover, prostacyclin may also increase the efficiency of the dialysis.

PROGRAM VISIBILITY

During the past year, the GCRC Program has continued to receive recognition as a vital component of the NIH clinical research effort. Centers throughout the Nation have continued to celebrate their 20th anniversaries with special events. These events have celebrated the scientific advances made possible with program support and have featured visits from distinguished scientists and Congressional leaders. The following institutions have held ceremonies celebrating their 20th year with the Program: Johns Hopkins University, Baltimore, Maryland; University of Southern California, Los Angeles, California; Yale University, New Haven, Connecticut; Washington University, St. Louis, Missouri; New York University, New York, New York; Duke University, Durhman, North Carolina; University of Rochester, Rochester, New York; Ohio State University, Columbus, Ohio; and Vanderbilt University, Nashville, Tennessee.

The number of research societies and public boards supporting the Program has increased. The National Diabetes Advisory Board has continued its support and strong endorsement of the Program and the National Digestive Disease Board has added its statement of support. The American Federation for Clinical Research, the Endocrine Society, the Society for Pediatric Research, the American Pediatric Society and the Association of Medical School Pediatrics Department Chairmen have all provided public testimonies on behalf of the Program. These public expressions of program support, together with the documentation of an impressive number of scientific advances made possible through these Centers, have served to highlight the contributions of the program to improving human health.

TABLE 1

ESTIMATED TYPICAL CENTER
(75 Centers)

FUNDED FY 82

8 beds

PERSONNEL	FTE	Amount (thousands)	
Professional	1.1	$ 70	
Administrative	1.4	27	
Laboratory	2.4	48	
Dietary	3.1	50	
Nursing	11.5	235	
Other 1/	.8	21	
Fringe Benefits (20.5%)		92	
	20.3		$ 543
HOSPITALIZATION			
Routine/Per Diem/Scatter Bed		$ 250	
675 B Patient Days X $119		(80)	
363 C Patient Days X $119		(43)	
1350 A Patient Days X $65 (Ancillaries)		88	
1275 Outpatient visits X $21 (Ancillaries)		27	
			242
TRAVEL			3
SUPPLIES, EQUIPMENT, OTHER			42
TOTAL DIRECT COST			$ 830
INDIRECT COSTS (8% of the Total Direct Costs)			66
TOTAL DIRECT AND INDIRECT COST			$ 896
LESS UNOBLIGATED BALANCE			(46)
			$ 850

1/ Includes 39.64 FTE Clinical Associate Physician positions.

Research Patients--Category A - Those patients admitted to the GCRC to participate in a research protocol.

Research Service Patients--Category B - Those patients admitted to the GCRC primarily for the purpose of diagnosis or treatment according to established procedures, and who are also participating in a GCRC research protocol.

Non-Research Patients--Category C - Those patients admitted to the GCRC solely for the purposes of diagnosis or treatment according to established procedures, and who are not participating in a research protocol.

Figure 1

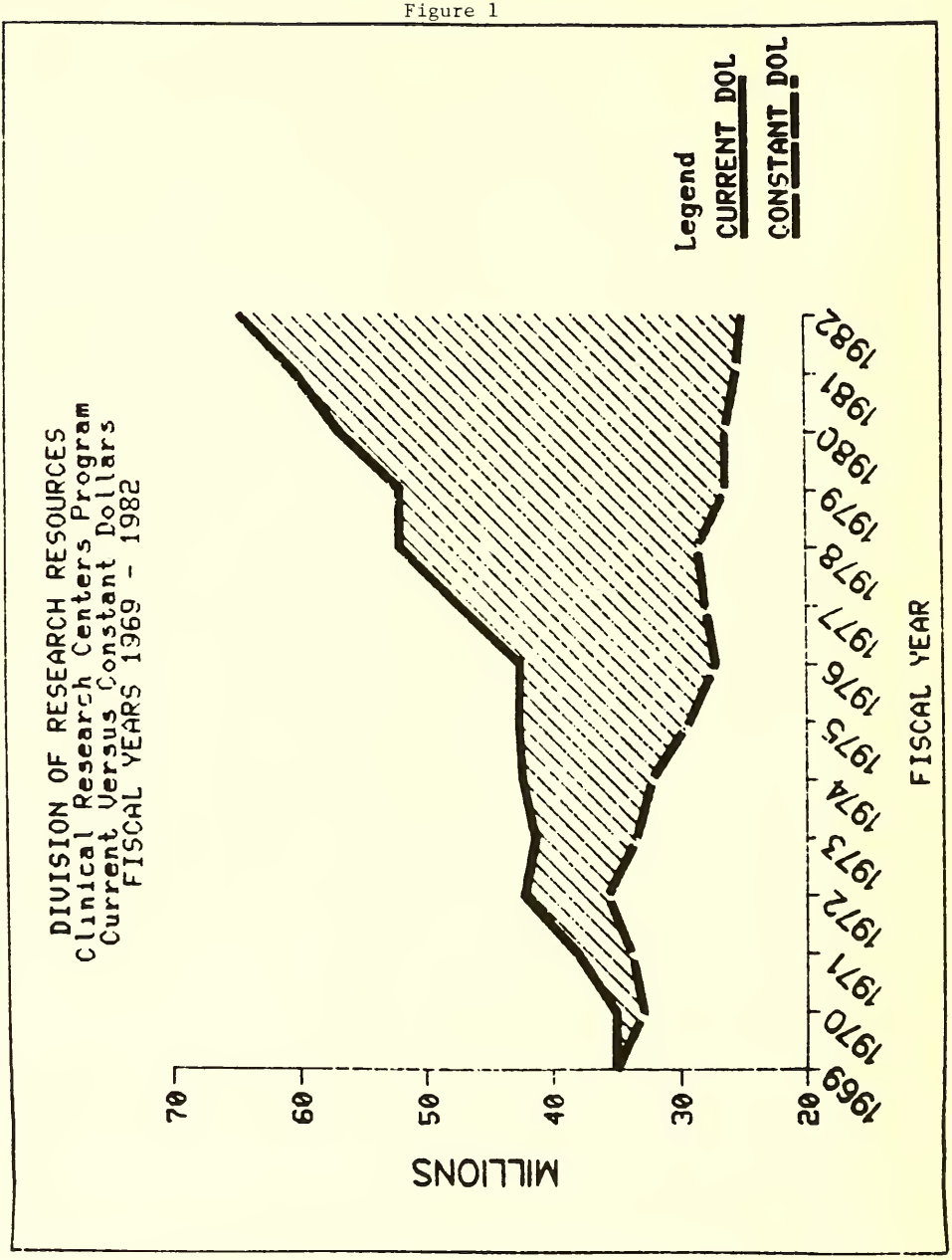

DIVISION OF RESEARCH RESOURCES
Clinical Research Centers Program
Current Versus Constant Dollars
FISCAL YEARS 1969 - 1982
Legend
CURRENT DOL
CONSTANT DOL
MILLIONS
70
60
50
40
30
20
1969
1970
1971
1972
1973
1974
1975
1976
1977
1978
1979
1980
1981
1982
FISCAL YEAR

TABLE 2

GCRC PROGRAM, 1969 - 1982

FY	CENTERS	FUNDED POSITIONS FTE	FUNDED BEDS	RESEARCH PATIENT DAYS A & B	OUTPATIENT VISITS
82	74	1,534	595	151,842 1/	95,447
81	75	1,555	592	151,679	108,053
80	75	1,694	602	164,634	101,966
79	74	1,640	613	171,365	86,215
78	79	1,708	633 2/	181,758	71,049
77	82	1,679	755	182,294	65,130
76	84	1,725	784	196,118 3/	56,217
75	84	1,719	823	200,988	50,020
74	87	1,808	877	208,263	50,614
73	83	1,790	893	207,084	36,280
72	84	1,867	907	221,642	23,654
71	82	1,885	881	216,455	14,515 4/
70	93	2,076	904	244,824	1,175
69	93	2,298	1,023	245,943	-

1/ Awarded
2/ Excludes 73 beds used for C patients included prior to 1977
3/ 12-month period
4/ FY 1971 - Initial year of outpatient program

TABLE 3

CLINFO & PROTOTYPES*

Grant Number	Institution	FY Funded
RR-54	New England Medical Center	82
RR-211	University of Tennessee	82
RR-827	University of California-San Diego	82
RR-43*	University of Southern California	81
RR-59	University of Iowa	81
RR-645	Columbia University	81
RR-833	Scripps Clinic	81
RR-888	Peter Bent Brigham	80
RR-585	Mayo Foundation	80
RR-400	University of Minnesota	80
RR-125	Yale University	80
RR-68	University of Cincinnati	80
RR-71	Mt. Sinai	80
RR-30	Duke University	79
RR-35	Johns Hopkins University	79
RR-37*	University of Washington	78
RR-95*	Vanderbilt University	78
RR-350*	Baylor University	78

TABLE 4

CLINFO & PROTOTYPES

FY	No. of GCRC Sites	Amount Awarded	No. of Commercial Sites
82	18	$1,421,267	3 1/
81	15	1,115,000	3
80	11	1,350,525	-
79	5	615,453	-
78	3	160,617	-

1/ 3 additional sites pending

TABLE 5

ESTIMATED PHS SUPPORT FOR INVESTIGATORS USING GCRCs BY INSTITUTE FOR FY 1980

Institute	Number of PHS Grants and Contracts Awarded to Investigators Using GCRCs	Awarded Dollars (Millions)
National Heart, Lung and Blood Institute	420	$120.1
National Institute of Arthritis, Metabolism and Digestive Diseases	630	94.1
National Cancer Institute	267	67.2
National Institute of Child Health and Human Development	166	31.9
National Institute of Neurological and Communicative Disorders and Stroke	93	24.1
National Institute of Allergy and Infectious Diseases	111	20.1
National Institute of General Medical Sciences	94	17.8
National Institute of Mental Health	66	5.9
National Institute on Aging	42	5.5
National Eye Institute	31	3.6
Other Public Health Service Support	38	3.8
National Institute of Dental Research	11	3.2
National Institute on Drug Abuse	18	2.2
National Institute of Environmental Health Sciences	9	1.7
National Institute of Alcohol Abuse and Alcoholism	17	1.3
Total	2013	$402.5

Biomedical Research Support Program
Division of Research Resources

Annual Report
Fiscal Year 1982
October 1, 1981 - September 30, 1982

Introduction

As we complete the second decade of the Biomedical Research Support Program (nee the General Research Support Grant Program), it is well that we reexamine and reflect on the following "Forward" which is quoted from the original published General Policy and Information Statement.

> "Strong and effective institutions are indispensable to the betterment of health care and to the improvement of fundamental conditions of human life. Educational and research institutions produce the scientific manpower, ideas, and techniques essential to the growth of concepts relating to health and disease and to the application of medical knowledge. Such institutions have a long and honorable tradition of providing intellectual encouragement and stimulation to creative scientists interested in fundamental problems, and of establising the surroundings and conditions in which such scientists can effectively conduct their research."
>
> "The General Research Support Grant Program is complementary to other forms of Public Health Service grants-in-aid. The purpose of the General Research Support Grant is to provide funds on a continuing basis to eligible institutions heavily engaged in health related research and research training, for their flexible and discriminating cultivation of disciplines of science relating to health. This grant permits institutions an increased measure of control over the quality, content, emphasis, and direction of their research activities. It permits them to recognize and support scientific talent earlier, and in general, to utilize funds flexibly and in ways that will be catalytic for fostering additional research capabilities and for attracting additional means of research support. The General Research Support Grant provides institutions unprecedented opportunities and responsibilities for cultivating scientific excellence and for building present and long-range institutional strength for health related research and research training."

Program Activities:

Biomedical Research Support Grant Program

As indicated in the FY 1981 Annual Report, changes were planned for determining a contemporary dollar level for the eligibility threshold, as well as the computation formula used for calculating the actual award to each

institution. For the FY 1982 determinations the computation formula was changed as follows:

15% of 1st $500,000 of "allowable" research grants base
plus
10% of $500,000 to $2 million
plus
6% of $2 million to $6 million
plus
0.6% above $6 million

Each individual total award was equal to the sum of the above increments times a proration factor which is a ratio of the total dollars available for the BRSG program to the total dollars computed by formula for all the BRSG institutions. The total number of institutions receiving BRSG support in FY 1982 dropped from 527 to 516. Thirty institutions receiving support in FY 1981 became ineligible as a result of their declining research grants base and some new institutions became eligible because of an increased research grants base. There was a slight shift upward in the levels of maximum and mean awards. This was a result of removing the maximum research grants base level used for computing the award.

Since the initial awards in 1962, the administrative definition of what constitutes an institution being "heavily engaged" in biomedical research has been based on an eligibility threshold equal to approximately five times the average cost of a research project grant (R01's) and/or 0.025% of the total NIH appropriation for research grants (these calculations yield similar values). Thus, the eligibility threshold in 1962 was $100,000. It was raised to $200,000 in 1976.

In the ensuing five year period the average cost of an R01 has increased by over 50%; the total research grants base of "allowable" grants used to compute the size of the BRSG award has increased 79%, and the funds appropriated for the BRSG Program have remained stable. The combined effects of these changes have been to reduce the size of BRSG awards to all BRSG grantees. The issue was discussed with advisors to the Division, including the National Advisory Research Resources Council, and a recommendation was made to and accepted by the Acting Director, DRR to raise the eligibility threshold to $500,000 in 1983. This threshold will ensure that BRSG awardees have a level of engagement in health-related research that is commensurate with the level that was required in 1960's and 1970's. This policy change was announced in November 1981. This policy was re-reviewed in May 1982 by the new Director, NIH and by the Assistant Secretary for Health, DHHS and reaffirmed.

The BRSG funds will be more appropriately allocated to those institutions most heavily engaged in conducting PHS-sponsored research. The change will reverse the five-year erosion of the size of the BRSG awards. The mean award from 1982 to 1983 will increase from $85,000 to $110,000 within an essentially flat appropriation (FY 1983 estimates). The threshold has been indexed at 0.025% of the NIH research grants appropriation. It will rise or fall with the total pool of available NIH research grant funding and, thus, avoid sudden shifts every five or more years.

Table I

Distribution of BRSG Awards by Size

Size of BRSG Award (in thousands)	Number of Grantee Institutions		
	FY 1976	FY 1981	FY 1982
Under $30.0	74	101	114
30 - 49.9	87	112	106
50 - 99.9	116	115	120
100 - 149.9	60	88	67
150 - 199.9	48	111	87
200 - 249.9	19	--	22
250 - 299.9	37	--	--
	441	527	516
Grant Range	FY 1976	FY 1981	FY 1982
Minimum	$17,418	$12,668	$11,383
Maximum	261,305	178,699	246,001
Mean	96,955	84,584	85,311

Table II

Distribution of BRSG Awards by Type of Institution

Type of Institution	FY 1976	FY 1981	FY 1982
Medicine	106	119	121
Dentistry	26	29	31
Osteopathy	1	1	2
Pub. Health	12	14	15
Pharmacy	13	27	25
Veterinary Medicine	10	12	12
Nursing	3	5	5
Optometry	0	2	2
Hospitals	63	62	63
Health Departments	2	2	2
Research Organizations	71	87	77
Other Academic	134	167	161
TOTAL	441	527	516

Illustrative Uses of BRSG Funds

One illustration of how Biomedical Research Support Grant funds have been used at a mid-western School of Medicine is the research project entitled "Myocardial Ethanol Metabolism". The researcher is a relatively new principal investigator whose prime appointment is in the Department of Medicine. In the study, the Principal Investigator notes that alcohol-induced heart muscle disease (AIHMD) is a prevalent disorder affecting about 200,000 Americans. The etiology of this syndrome has not been elucidated, due in large part to previous thinking that the heart does not metabolize ethanol directly. For the first time, intermediate products of myocardial metabolism of ethanol were identified. These products (fatty acid ethyl esters) were isolated and identified in rabbit hearts. These esters have also been identified in human myocardium in men who have suffered traumatic deaths. It has been demonstrated that these esters are made enzymatically in several organs including the heart, aorta, pancreas, and liver, but they are not made significantly in skeletal muscle or the brain. Furthermore, it has been shown that these esters inhibit cholesterol esterification in both the liver and aorta. These findings may help to explain, at least in part, the triglyceride accumulation in AIHMD and the apparent diminished atherosclerotic effects found in daily, moderate consumers of alcohol. This research has been published in the Journal of Biological Chemistry. Other manuscripts concerning the research are in preparation. BRSG funds have served to support the investigator's research by allowing this investigator to partially equip his research laboratory and to purchase supplies to allow for the work on the project.

Another example of the use of BRSG funds for the support of an investigator is taken from the progress report of a western university. The initial equipment which was obtained for the investigator's laboratory shortly after the arrival at the University was purchased using funds provided by the institution's Biomedical Research Support Committee. The equipment included a centrifuge with rotor, a dispersal unit with generator, a special pH meter, and a temperature controlled heating block. The equipment enabled the investigator to begin research on prostaglandin synthesis in amphibian bladders and obtain initial data on adenylate cyclase activity of frog membrane preparations. He used this pilot data to write grant proposals to the National Science Foundation, and the local Affiliate of the American Heart Association. Both proposals were funded in 1981, the NSF grant for $60,000 and the local affiliate grant for $5,777. The prostaglandin synthesis data have been published in Prostaglandins and the adenylate cyclase data is in press in General and Comparative Endocrinology (1983). Thus, the funds which the local BRS Committee provided were extremely useful in setting up the laboratory, obtaining initial data which assisted in obtaining funding, and which was utilized in subsequent publications.

A final example of an institution's use of BRSG funds is from an eastern medical center where an investigator received an "approved but not funded" on his NIH renewal application. BRSG funds administered by the Center allowed the investigator to continue the work on basic mechanisms involved in the property of certain heart medicines to produce toxic arrhythmias and how the nervous system is involved in facilitating such arrhythmias after heart attacks. The investigator was able to obtain sufficient additional data to allow revision of the proposal and received an approval with funding for the renewal request.

Shared Instrumentation Grant (SIG) Program:

The SIG Program was initiated in FY 1982 with the objective to make available, to institutions with a high concentration of NIH extramural research awards, research instruments which can only be justified on a shared use basis and for which meritorious research projects are described. A total of 203 applications were reviewed requesting 38.7 million dollars. The list of requested instruments included electron microscopes, cell sorters, nuclear magnetic resonance spectrometers, mass spectrometers, automated peptide synthesizer -- amino acid analyzers and other highly sophisticated instrument systems.

Of these requests 176 were recommended for approval with a budget of $29,568,478. Twenty three meritorious requests were funded with an aggregated budget of 3.7 million dollars.

The announcement for the second year (FY 1983) of the SIG program appeared in the NIH Guide for Grants and Contracts, Vol. 11, No. 7, June 18, 1982.

In FY 1983, eligibility is limited to those grantees which received a BRS grant award in FY 1982. NIH records will be used to verify eligibility. Only one application for a single shared instrument may be submitted by each eligible BRS grantee in a review cycle. Applications will be received only once per year. The program is highly competitive. The President's Budget for Fiscal Year 1983 requests $5.0 million for the program. At this funding level, it is expected that a minimum of 20 and a maximum of 66 awards would be made in 1983. Future funding is contingent on the availability of appropriated funds.

Biomedical Research Development Grant Program

The BRDG Program was initiated in FY 1977 with the objective to strengthen and/or expand health-related research in new, small and developing institutions provided it would result in improving the training of manpower for clinical health professions or health-related research or both. The last deadline for acceptance of applications was October 1, 1979 with the FY 1980 being the last period for making new awards. A total of 42 institutions have been funded over the tenure of the program with the final 10 institutions receiving their third and last year of support from the program in the FY 1982. Seventeen institutions have submitted their final progress reports. Of the 42 institutions receiving BRDG support it would appear that six could probably and two possibly meet the new threshold requirement of having a Research Grants Base of $500,000 and be eligible for BRSG funds in FY 1983. Nineteen of the 42 institutions are receiving BRSG funds in FY 82.

Biomedical Research Support Program - Major Issues

As authorized by Public Law 86-798, The Biomedical Research Support Program (nee General Research Support) funding level ceiling was set at up to 15% of the total National Institutes of Health appropriation for research grants. By the late 1960's the level was averaging almost 8%; by the first five years of the 1970's it averaged 6.4%. A precipitous decline occurred during

the second five years of the decade to an average of 2.9%, and during the first four years of the 1980's the level has dropped still further to an average of 1.9%.

In 1958, the Panel on Research Policy of the President's Science Advisory Committee in a report to President Dwight David Eisenhower, entitled "Strengthening American Science," stated --

> "With increased Federal funds flowing to research activities outside of Government, it is important to continue and strengthen the project system, but other instrumentalities should be used to supplement the project system."
>
> "...institutional grants would permit more effective research in broad areas of science and provide greater freedom for the scientific community to give direction to the work undertaken. They might also prove to be an important administrative device for reducing the potential growth of Government administration..."

In 1965, an NIH special report to the Bureau of the Budget, entitled "Use of the General Research Support Authority," stated --

> "The concept of providing flexible, general research support for institutions engaged in biomedical research has evolved both from long discourse between the Federal government, investigators, and organizational entities, as well as out of the crucible of experience acquired over a number of years in which this type of institutional support was not available. The flexibility inherent in the concept of breadth of the GRS authority provides an unparalleled opportunity for innovation and creative administration. Utilization of this authority should enable the NIH to carry out more effectively its statutory missions and meet the expectations of the Congress and the public for a maximum return on the Federal investment."

Out of the concept of institutional grants of the late 1950's and the promise of the mid-1960's there has been the development by the Division of several competitive grant programs to serve different purposes and different types of institutions. Several have been time limited, and others are still needed and still functioning quite well.

Superimposed upon this time span of concept, promise and development has been the steadily eroding fiscal base to support and further execute the concept.

In the last few years a different variant of stress has appeared. There have been diminished fiscal resources allocated to DRR to exploit what the NIH report to BoB described in 1965 as "an unparalleled opportunity for innovation and creative administration" or even to sustain some of the fundamental functions of the original General Research Support Grant Program. Since the 1950 concept still retains its validity in the 1980's there is a trend toward development by individual elements of the NIH to use substitute methods to gain somewhat

similar ends. Examples of various activities that have emerged or are currently being considered are as follows:

- In a May 1982 report, entitled "Collected Experiences with Small Grants Programs at the NIH and NIMH" it described the situation where from 1956 until the early years of the next decade, most of the Institutes participated in Small Grants Program. When the General Research Support (GRS) Program was initiated in 1962, small grants were eliminated from the Institute's repertoire of funding mechanisms. The justifications for small grants are to fund pilot projects for unique or innovative studies, to help young investigators into the grants process, and to enable investigators whose research careers were interrupted to resume research. A criticism aimed at the small grants program of the individual Institutes at that time was that it was not cost effective with respect to review and grants management expenses. Accordingly, all grants which were for $2,000/year, or less, were to be referred to the GRS Program for possible funding.

- In 1974, categorical Institute interest in small grants was briefly rekindled as a result of the President's FY 1975 budget which did not specify funds for the GRS Program. Congress, however, reinstated the Program. Although the name was subsequently changed to the Biomedical Research Support Program, the funding mechanism is still in place. However, in the last few years, with the continuing difficulty of DRR to sustain "small grants" of the dollar size warranted by the needs of the 1980's, interest in small grants has been enthusiastically renewed to the extent where active programs have been initiated by three categorical Institutes: NEI, NIA, NIDR.

- At the May 1982 meeting of the National Cancer Advisory Board it was proposed that 1% of the NCI budget be targeted for decentralized peer reviews to be carried out by approved research institutions for innovative pilot projects. The proposal was described as "an Institute equivalent of the Biomedical Research Support Grants."

Each of these different activities can be viewed as an erosion of the centrality of the use of general research support authority; could set in motion a series of independent and uncoordinated actions by the individual Institutes seeking substitute devices, and eventually lead to the weakening of the Biomedical Research Support Grant Program. A program considered so valuable that it has prompted more than one Dean of a major medical school to state --

> "I regard the BRSG so important that I would advocate reduction in the amount given for individual grants before I would cut the already greatly reduced BRSG."

Thus, we are faced with the dilemma of the steadily decreasing capacity of the BRSG to be responsive to the increased need and demand for institutional funds for biomedical research for use in a localized decision making mode, and a variety of NIH actions that could possibly lead to eliminating that capacity altogether.

An evaluation of the multiplicity of views and values placed on the Biomedical Research Support Grant Program by NIH scientist-administrators, present and former recipients of BRSG funds, National Professional Organizations and policy makers at both the Executive and Legislative Branches of the Federal Government would prove valuable as a basis for charting the future direction of use for the general research support authority ascribed to the NIH by Public Law 86-198 over 20 years ago. The early phases of developing a work scope for the initial phases of such an evaluation are currently underway.

FISCAL YEAR 1982
ANNUAL REPORT
MINORITY BIOMEDICAL RESEARCH SUPPORT PROGRAM
DIVISION OF RESEARCH RESOURCES

PROGRAM DESCRIPTION

Background

The Minority Biomedical Research Support (MBRS) Program was established in response to the recognition of the severe underrepresentation of minority individuals in biomedical research.

To assist in correcting these deficiencies, in Fiscal Year 1972, under the authority of Section 301(c)--now 301(a)(3)--of the PHS Act, as amended (42 U.S.C. 241(d)), the Division of Research Resources (DRR) initiated the Minority Schools Biomedical Support Program. It was later renamed the Minority Biomedical Support (MBS) Program. The program is focused on colleges, universities, and health professional schools where 50 percent or more of the students were classified as minority. Other institutions including those on Indian reservations having substantial minority enrollments (but less than 50%) and demonstrating special commitment and assistance to minority faculty and students are also eligible. The Program was expanded in 1975 to include two-year institutions. In February of 1982 the Program was renamed the Minority Biomedical Research Support (MBRS) Program. On the advice of the Program Directors and the Advisory Committee the name of the program was revised to emphasize the fact that this is a research program and avoid its being referenced as a training program.

Mission

The MBRS Program seeks to relieve the shortage of minorities engaged in biomedical science research by strengthening institutional research capabilities and promoting faculty and student research participation at eligible institutions. The expected result of MBRS initiatives will be a cadre of minority scientists who will contribute significantly to the evolving base of knowledge in the health sciences.

Objectives

The overall objective of the MBRS Program is to increase the number and quality of minority biomedical research scientists. This is accomplished through the following interrelated thrusts:

- The strengthening of the capability of eligible institutions to support the conduct of quality research in the health sciences.
- The support of faculty at eligible institutions as they initiate or expand their biomedical research interests and capabilities.
- The support of minority students on research projects at the undergraduate and graduate levels in order to motivate and prepare them for careers in biomedical research.

SCIENTIFIC ACCOMPLISHMENTS

In general the quality of science at the institutions supported by the MBRS Program and the productivity of the MBRS investigators have continued to improve. When the Program was launched the projects were very general in nature and restricted to basic biological studies. In contrast, the present portfolio of projects are more specific in a variety of biomedical areas of research such as: the use of recombinant DNA technology, vaccine development, clinical studies on hypertension, development of new drugs, and pharmacokinetics.

Faculty Participation

A total of 610 faculty participated in 521 projects during 1982. The research accomplishments of 1981 included 683 scientific papers published by faculty and students and 761 faculty presentations. For comparison purposes Figure I shows trends from 1974 to 1981.

Not all the data are available yet for FY 1982 on accomplishments, but 61 grantee reports show that there were some significant research accomplishments. The following are examples of research accomplishments being carried out at MBRS-supported institutions:

Dr. Stanley Evans, Department of Pharmacology at Meharry Medical School has recently synthesized several analogs of anti-hypertensive drugs. Preliminary testing has shown that these substances have few of the adverse effects associated with several compounds which are already on the market. Dr. Evans did his graduate work at Howard University and was one of the first MBRS participants to receive the Ph.D. degree. He carried out postdoctoral studies under a National Research Service Award in the Laboratory of Chemistry under Dr. Henry Fales of the National Heart, Lung and Blood Institute at NIH before accepting a position at Meharry.

An investigator in the Department of Natural Sciences at Medgar Evers College and collaborators at the Albert Einstein College of Medicine have been the first to demonstrate that there are drug binding sites in the pedal ganglia of the marine mollusc Mytillus edulis. The nervous system of this invertebrate is considerably less complicated than mammalian systems but is a good model for monitoring cellular and electrical changes induced by drugs. The investigator chaired a session and reported on his research at the XXVIII International Congress of Physiological Sciences in Budapest, Hungary in July 1980 and presented new research findings at the International Congress on Comparative Neuropharmacology which was held in Japan in 1981.

Sickle cell anemia is transmitted genetically by a recessive gene and thus the disease state only manifests itself when the alleles for normal hemoglobin are absent. In the United States about 5-8% of the Black population are either affected by sickle cell disease or are carriers of the trait. This disease is found among the populations over all of tropical Africa, in India, Arabia and southern Europe. In an attempt to better understand the sickling phenomenon associated with sickle cell anemia, Dr. John K. Haynes, an investigator in the Biology Department at Morehouse College in Atlanta, Georgia, is attempting to characterize irreversibly sickled cells (ISC). Comparisons are being made between the protein organization of the ISC cytoskeleton and the normal RBC's

using crosslinking techniques, various extraction procedures, electrophoresis and electron microscopy. The ultimate goal is to isolate and characterize specific sites on the external surface of the red blood cell membrane. These studies could lead to a better understanding of and hopefully a treatment of sickle cell anemia.

Investigators at Bishop College, an undergraduate institution in Dallas, have developed a rapid (four minute) procedure using radioactive Iodine^{125} to qualitatively and quantitatively determine the molecular weight of RNA samples. This rapid iodination procedure, when combined with two-dimensional gel electrophoresis, simplified identification of RNA without interference from impurities.

At Howard University, an investigator is carrying out research on breast tumor growth. By studying mammary cancer induced in laboratory rats by a carcinogenic agent, he is beginning to delineate the role of hormones and certain hormone inhibitors on the rate of tumor growth. His work is based on the observation that approximately 40 percent of the mammary carcinomas occuring in American women appear to be hormone dependent. Recently it was demonstrated in this laboratory that the compound CI-628, a female hormone antagonist which competively binds to hormone receptors, induces tumor regression and terminates the synthesis of an important catalyst in tumor cells. It was also shown that another female hormone antagonist, progesterone, results in a blockage of the biological processes involved in tumor development.

Biologists at the University of Puerto Rico, Rio Piedras campus, are developing a vaccine against schistosomiasis, a parasitic disease which affects 10 to 15 percent of Puerto Ricans and over 200 million people in tropical areas throughout the world. Tests of a new vaccine, isolated from a related parasite, Fasciola hepatica, which infects the livers of cattle and sheep, gave a significantly higher degree of protection than has been obtained using other methods. Efforts are continuing to improve the vaccine to achieve at least 80% protection consistently, to identify all the protective antigens and optimize treatment regimens and, eventually, to test the vaccine in non-human primates. Dr. George Hillyer, an investigator in the College of Natural Sciences at the University of Puerto Rico, Rio Piedras, received the Henry Baldwin Ward Medal for 1982, for his outstanding contributions in schistosomiasis research. The award is the highest research award which the American Society of Parasitologists bestows on its members. Dr. Hillyer gives credit to the MBRS Program for getting him started and assisting him in developing his career.

Student Participation

Approximately 5,600 minority students have participated in the Program since 1972. All of the Progress Reports for FY 1982 have not been received but the data available from 76 grantees shows that a total of 904 undergraduate and 328 graduate students participated in the Program in 1982. The FY 1981 graduates made the following career choices: dental school, 17; medical school, 131; graduate school, 151; other health related schools, 83. The students who did not pursue advanced studies are employed largely in jobs related to health. (See Figure II)

At 10 MBRS eligible institutions, approximately 60 minority students received their Ph.D. degrees while participating on MBRS-funded projects. They are currently engaged in biomedical research, either at the postdoctoral or faculty level.

Howard University - The MBRS Program has supported 392 students at Howard University during the period 1972-1981. The student participants from 1972-1981 include: 169 undergraduates, 179 graduates, 13 dental students, and 31 medical students. In 1979, 15 were in graduate school pursuing a Ph.D., 34 were in medical school pursuing a M.D., 1 was in veterinary school, 2 were in dental school, 88 did not pursue advanced degrees in biomedical sciences, but hold jobs as teachers, technicians, etc. As of 1979, a total of 151 have completed their undergraduate degrees: 14 completed the Ph.D., 21 completed the M.D., and 27 completed the D.D.S.

University of New Mexico - During the first five years of the MBRS Program (1973-1978) over 210 students have participated; 101 have been awarded degrees at University of New Mexico, including 19 Masters, 5 Ph.D.'s, and 3 M.D.'s. They currently have 70 undergraduate and 9 graduate students participating in 41 faculty research projects. Last year the students attended and presented papers at 10 national meeting of scientific societies and one international meeting. Dr. L. E. Davis was an invited speaker at the World Congress of Neurology-Kyoto, Japan to discuss an experimental model of Reye's Syndrome. He has developed a research model with influenza virus that shows promise in the studies of Reye's syndrome.

Meharry Medical College - Only graduate students participate on MBRS funded projects at Meharry. There have been 15 students who graduated with a Ph.D. to date. One of them has elected to go for the M.D. degree and the others are in biomedical research careers. Several are in postdoctoral positions at NIH, Harvard, University of California and other leading universities. Others are in faculty positions at other colleges and universities. There are presently 22 graduate students supported by the MBRS Program at Meharry and all are pursuing the Ph.D. degree.

University of Puerto, Rio Piedras - More than 240 students have participated on the MBRS Program since it began in 1973. Of these, approximately 100 have obtained the B.S. degree, 30 have obtained the M.S. degree, and four have obtained the Ph.D. degree from the University of Puerto Rico. A number of these graduates have entered medical, dental and graduate schools. Others are currently employed as teachers and researchers in facilities which are located primarily on the Island of Puerto Rico. The 25 faculty participants are currently involved with 109 students (72 undergraduates and 37 graduates). These students have made over 60 presentations at scientific meetings, and have been included as co-author on some of the 93 publications from these laboratories in the past year.

Meetings and Conferences

The 10th. Annual MBRS Symposium was held in Albuquerque on April 3-6, 1982. About 1,500 students, faculty and other participants attended, including a large contingent of staff from the various Institutes at NIH and ADAMHA. There were 474 papers presented in the poster and slide sessions at the meeting by students and a few faculty. Workshops in the following areas were conducted:

alternate sources of funding; alternatives to academic careers; careers in academic medicine; careers in basic science. During the meeting symposia were convened on "Metalloproteins" and "Endocrinology". Two invited lecturers, Dr. Julius Jackson of Meharry Medical College and Dr. J. Donald Capra of the University of Texas Medical Center, Dallas, gave presentations on "Genetic Engineering" and "Hybridomas", respectively. This year the guest speakers were selected from the MBRS participating faculty as part of the celebration of the 10th. anniversary of the Program. Dr. James Henderson of Tuskegee Institute gave the keynote address on the historical aspects of the Program. Dr. Don Anshapanek of Haskell Indian Junior College gave the banquet address entitled, "What it takes to be a winner."

Six $500 awards of excellence for research and presentation were given to student scientists at the 1982 10th. Annual Minority Biomedical Research Support Symposium held in Albuquerque, New Mexico. The student scientists were judged by a select committee of scientists headed by Acting DRR Director, Dr. James F. O'Donnell. The award winners were Eduardo Acosta of California State University at Los Angeles; Bobby Burkes of Atlanta University Center; Sergio Coronado of the University of Texas at El Paso; Rosilyn Howard of Florida A&M University; Joe Reyes of San Jose State University; and Sharon O. Williams of Meharry Medical College.

As part of the Program efforts to assist faculty in developing competitive research grant applications, the staff collaborated with the National Institute of Mental Health (NIMH) in conducting two grantsmanship workshops in 1982. These were specifically targeted for investigators in the benavioral and social sciences. The intent was to increase the number of subprojects that can be co-funded through the Intra-Agency Agreement with NIMH. About 50 investigators participated in the two workshops. Staff of the NIMH continue to keep in contact with them as they develop research grant applications.

Annual Program Directors' Meeting

This year the meeting was held in Washington, D.C. at the National 4-H Center. The major business item for the meeting was discussion and commenting on the policy document, "Alternatives for Reviewing MBRS Applications." The grantees provided the staff with meaningful input that was most helpful in developing a set of alternatives that grantees and staff can work with while conducting the review of applications.

A featured speaker, Mr. Harley Dirks, former Chief-of-Staff for the Senate Appropriations Committee, provided the participants with an excellent overview of the congressional operations. The program directors and staff agreed to hold the next meeting in Washington, D.C. again.

Strengthening the Technical Merit Review

In achieving the Program goals this year, the staff worked with the Advisory Committee, the National Advisory Research Resources Council and grantees to develop alternate options for reviewing the variety of applications received from the many different types of institutions. The study and discussions resulted in a program policy document to be used as a guide in the review of MBRS applications. As reported last year, one of the options implemented was the use of panels of experts to review subprojects in each of

several general disciplines such as, immunology, biochemistry and psychology. Several panel reviews have already been conducted and the procedural problems are being resolved. These and other management changes are designed to effect a more efficient use of our resources and distribute the workload more evenly throughout the year.

Cofunding and Cost-Sharing with Other Programs

As a further expansion of its impact, the MBRS Program established an administrative mechanism in Fiscal Year 1975 for involvement of other Institutes of NIH in funding some of the research projects occurring in MBRS-supported institutions. The majority of the NIH Institutes, and the National Institute of Mental Health (NIMH) in ADAMHA are presently engaged in these agreements with the MBRS Program. Such arrangements permit the cooperating Institute to pay the costs for projects which are of direct concern to their stated missions and assist the principal investigators in gaining individual research grant support from the categorical Institutes. The MBRS Program provides for the overall review and management of these projects, including budget negotiations and monitoring of progress and accomplishments. The following table illustrates the cofunding activity to date in FY 1982.

Cofunding and Interagency Agreements Activity
FY 1982

Institute	Funds	No. Projects
NCI	$1,894,756	32
NHLBI	1,707,497	38
NIAID	85,989	2
NIADDK	1,199,640	41
NIDR	55,352	1
NIA	148,848	4
NEI	121,430	3
NICHD	328,181	9
NINCDS	146,460	6
NIEHS	112,111	1
NIMH	870,000	17
GCRC (DRR)	100,000	—
TOTALS	$6,770,264	156

Program Planning

A revised planning document (updated 5-Year-Plan) is being developed. This document outlines the needs and opportunities, specifying goals and planned actions for the mid 1980's. The major goals will be:

- Expanding activities to enhance institutional biomedical research capability in institutions that show need and promise.

- Expanding research career enrichment opportunities for faculty.

- Recognizing that a significant number of MBRS graduates enter medical school, the Program will continue to encourage and motivate these students to choose biomedical research careers instead of private practice.

The Advisory Committee and Council identified specific areas of high priority that required planned actions in the next five years in order to carry out the goals of the Program. These initiatives are listed below in priority order.

- Instrumentation Awards

  MBRS institutions share the same problems of obsolescence of equipment and growth in capabilities as others in the biomedical research community. The Program funded its first grants in 1972 and some of the institutions have developed their research enterprise to a point requiring new items of large equipment and replacement of obsolete equipment. The MBRS institutions are experiencing great difficulty in maintaining or increasing the momentum gained in biomedical research, because of the highly competitive arena for other sources of funds by the entire research community.

- Facilities Improvement

  As the biomedical research capability increases at some MBRS institutions, there is a dire need for upgrading and renovating animal care facilities and laboratories.

- Faculty Research Career Enrichment

  Ordinarily, faculty at smaller and also in isolated MBRS institutions do not have the opportunity for much interchange with active researchers in their discipline. There is a need to provide opportunities for them to spend 3-5 months off campus at a research intensive laboratory. Many times this is necessary prior to starting a project or for retooling, learning new methods, or being brought up-to-date on current scientific developments.

- Student Initiatives

  In many MBRS institutions, little opportunity exists for students to interact with researchers other than their mentor. Other factors that motivate students for biomedical research careers are lacking due to the isolation or the size of the institution. Our limited experience in sending some of these students off campus during summers to NIH laboratories and other major universities has demonstrated that this is a most rewarding investment. In order to provide these students with more opportunity for research exposure, summer research experiences are proposed. Salaries, as well as travel support, would be provided for students to spend a summer at a laboratory in a major research setting. Over the years, the MBRS Program has graduated 1,500-2,000 students who have entered professional schools of medicine, dentistry, veterinary medicine, and other health professions. Many of these students continue their interest in research but find it difficult to obtain research support. The Program hopes to provide support for these students, on a pilot basis, to engage in research during their "off" quarters or summers. The eligibility would be based on prior MBRS participation. Payments would originate from the MBRS home institution.

- Collaborative Activities

  The current planning for collaborative efforts is geared to:

  Provide for established scientists at major institutions to visit MBRS schools on an extended or long-term basis in collaboration with the Minority Access to Research Careers (MARC) Program of the National Institute of General Medical Sciences.

  Provide for co-funding of training activities, also possibly in collaboration with the MARC Program.

  Increase collaboration with the private sector. The MBRS Symposium might be used as a mechanism to initiate interactions with pharmaceutical, chemical and other companies with MBRS investigators.

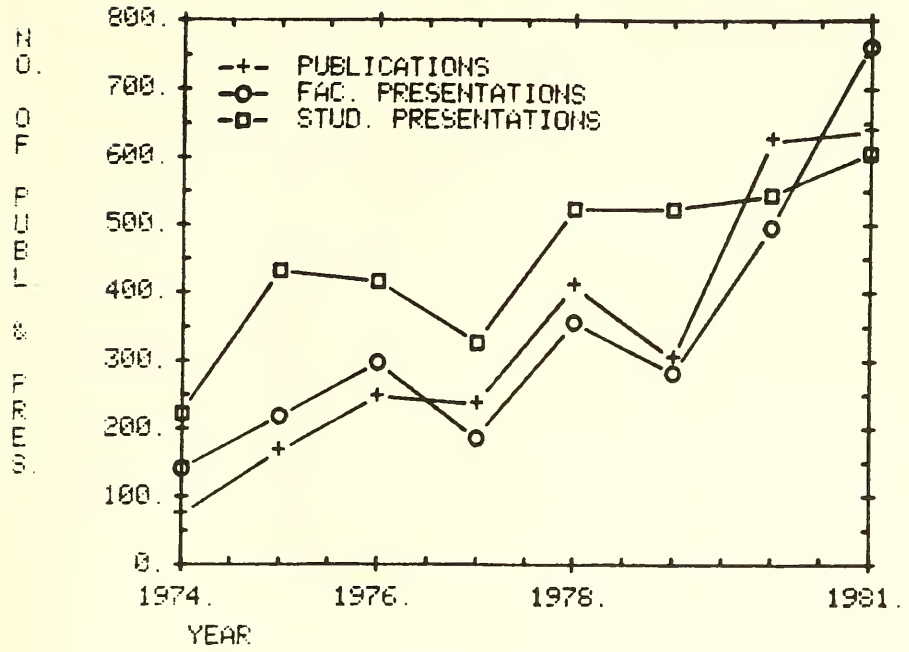
  Develop collaborative partnership between the MBRS Program and the local community.

Program Evaluation

The contract for a short-term evaluation of the Program was let on September 1, 1982 to the Triton Corporation. The evaluation team has been interviewing NIH personnel who are knowledgeable about the Program as well as some people outside the government. They will be submitting a preliminary report on October 15, 1982. They are preparing a revised program summary which will incorporate the perspective gathered from all the people interviewed and the evaluators' perspective of the Program from a study of the Program, grant files and other documents. A second stage of the evaluation will involve a close look at the data in the files and an analysis of this data. The result of this would be some suggestions for Program decisions and a plan for a longer term evaluation.

FIGURE I

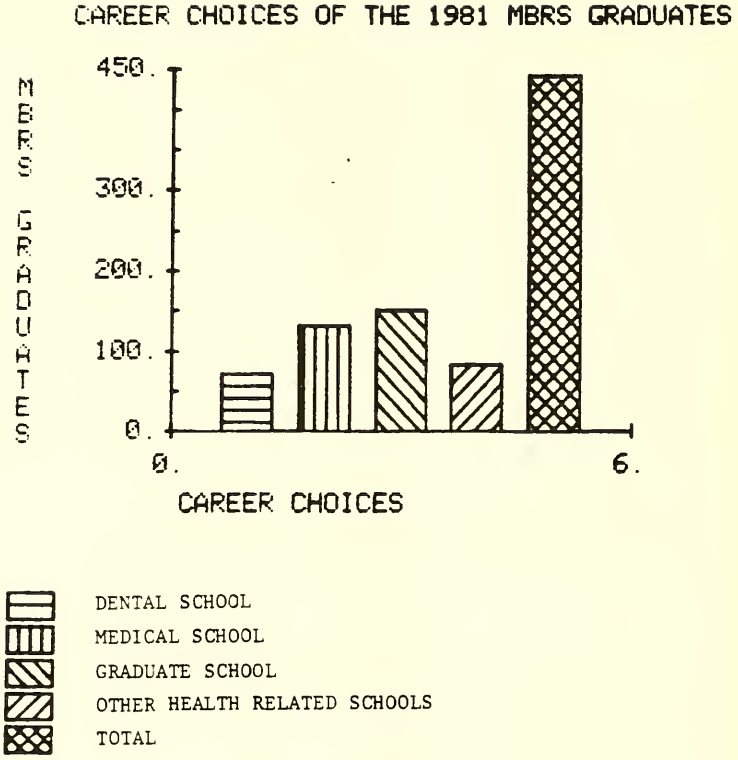
RESEARCH ACCOMPLISHMENTS TRENDS: 1974-1981



NO OF GRANTEES AND NO. OF PROJECTS FOR WHICH DATA ARE REPORTED EACH YEAR:

0 YEAR	1 NO.OF PROJECTS	2 NO.OF GRANTEES
1. 1974	314.	63.
2. 1975	408.	69.
3. 1976	378.	75.
4. 1977	257.	74.
5. 1978	318.	71.
6. 1979	380.	71.
7. 1980	488.	79.
8. 1981	486.	79.
9. 1982	521.	78.

FIGURE II


CAREER CHOICES OF THE 1981 MBRS GRADUATES
MBRS GRADUATES
450.
300.
200.
100.
0.
0.
6.
CAREER CHOICES
DENTAL SCHOOL
MEDICAL SCHOOL
GRADUATE SCHOOL
OTHER HEALTH RELATED SCHOOLS
TOTAL

OFFICE OF GRANTS AND CONTRACTS MANAGEMENT

The Office of Grants and Contracts Management (OGCM), Division of Research Resources, continued to play an important role in the review, negotiation, award making, and the administration of the Division grant programs, as well as aiding in the administration of research and development (R&D) contracts that are made by the Research Contracts Branch, Division of Contracts and Grants. During FY 1982, a total of $186,729,000 was awarded, of which 1,154 were grant awards in the amount of $181,854,000, and 22 contract actions in the amount of $4,875,000.

During March of 1982 OGCM began using the Interactive Awards System. This system allows the Notice of Grant Awards to be prepared within OGCM by using a CRT terminal and printer. The new process has greatly expedited the making of DRR grant awards. The new process is being used for all DRR Programs with the exception of awards that involve co-funding. A large number of Minority Biomedical Research Support awards involve co-funding. The Division of Research Grants has not completed the necessary programming that would allow awards that have co-funding to be processed under the Interactive Awards System.

The following tables and charts reflect the total DRR grant and R&D contract effort for FY 1982. Particular attention is invited to the chart titled "Division of Research Resources Research Grant Award in Current & Constant Dollars Fiscal Years 1972-1982." It should be noted that the downward trend of constant dollars compared to current dollars is still continuing.

DIVISION OF RESEARCH RESOURCES
FY 1982 OVERVIEW OF GRANT AND R&D CONTRACT PROGRAMS

Program	Funding	Major Resources Supported
General Clinical Research Centers Program	$ 63,899,000	• 75 General Clinical Research Centers (Includes two phase outs) • Over 3300 Research Projects • 39 Clinical Associate Physicians • 18 CLINFO Sites; 1 Contract
Biotechnology Resources Program	$ 21,517,000 1/	• 57 Biotechnology Resources 16 Knowledge Engineering and Information Technology in Biomedicine (3 contracts) 9 Biomedical Engineering and Digital Technology 32 Technologies for Study of Biomolecular and Cellular Structures and Function
Animal Resources Program	$ 26,155,000 2/	• 7 Primate Research Centers, including 220 Core Research Projects • 7 Primate Breeding Projects • 62 Animal Research and Resource Project Grants and Contracts • 12 Training Programs
Minority Biomedical Research Support Program	$ 24,568,000 3/	• 80 Institutions • 521 Research Projects • 610 Faculty, 909 Undergraduates, and 330 Graduate Students • 5 Prophet Sites Minority Symposium
Biomedical Research Support Program	$ 49,395,000	• Biomedical Research Support Grants to 516 Institutions • Development Awards to 9 Institutions • Minority High School Research Apprentice Awards for 644 Students • Shared Instrumentation Award to 23 Institutions
Office of the Director	$ 1,195,000 4/	• Culture Collection and Research Resources Reporter Contracts
Total Funding	$ 186,729,000	

1/ Includes $1,318,000 ($724,000 other than Program appropriated funds and $594,000 from other DRR Program funds for Scientific Evaluation Grant)
2/ Includes $ 95,000 other than Program appropriated funds
3/ Includes $6,782,000 " " " " "
4/ Includes $ 695,000 " " DRR " "

OGCM FY-1982

DRR FY 1982 GRANT AND R&D CONTRACT AWARDS BY MECHANISM

(Dollars in Thousands)

PROGRAM ACTIVITY	Research Grants: Research Centers			Research Grants: Other Research			Training Programs			R&D Contracts		
	Type	No.	Amount	Type	No.	Amount	Type	No.	Amount	Type	No.	Amount
General Clinical Research Centers Program.....		M01s			R13s							
	1	2	$ 934	1	1	$ 41				New		--
	2	15	9,754							Mod.	1	$ 24
	3	16	642									
	5	59	52,504									
		92	$63,834									
Biotechnology Resources Program.....		P41s			P09s							
	1	6	$ 2,872	3	1	$ 594				New		--
	2	4	1,680							Mod.	3	$3,051 1/
	3	11	1,864		R13s					Intra/		
	5	30	8,910	1	5	$ 54				Inter	2	153
		51	$15,326		R23s						5	$3,204
				5	1	$ 58						
					R24s							
				1	3	$1,285						
				3	2	92						
				5	3	904						
					8	$2,281						
Animal Resources Program.....		P40s			R24s			F32s				
	1	12	$ 1,070 2/	1	1	$ 88	1	1	$ 22	New	1	$ 71
	2	3	615	2	2	194	5	1	18	Mod.	6	381
	3	9	313	3	2	46		2	$ 40		7	$ 452
	5	27	4,004	5	5	279		T32s				
		51	$ 6,002	7	1	15	1	1	$ 63			
					11	$ 622	2	4	332			
		P51s					3	1	64			
	2	1	$ 3,067				5	3	168			
	5	6	15,332					9	$ 627			
		7	$18,399 3/					T35s				
							5	1	$ 13			

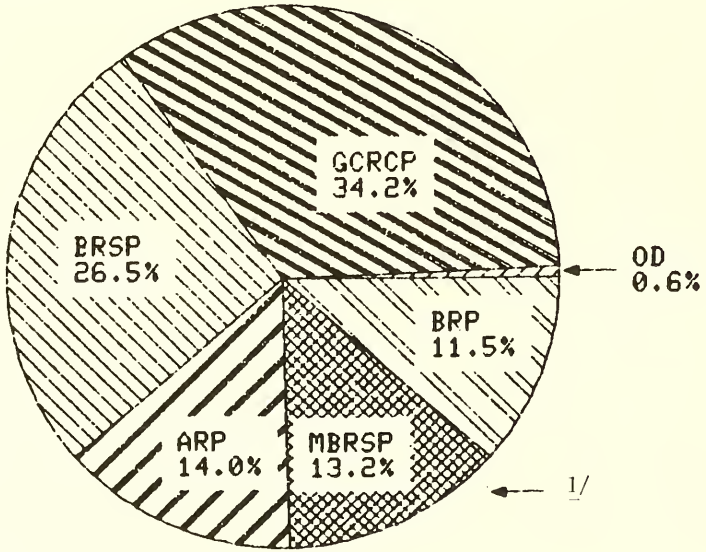
OGCM FY-1982

DRR FY 1982 GRANT AND R&D CONTRACT AWARDS BY MECHANISM (CONTD)
(Dollars in Thousands)

	Research Grants									R&D Contracts		
	Research Centers			Other Research			Training Programs					
	Type	No.	Amount	Type	No.	Amount	Type	No.	Amount	Type	No.	Amount
Biomedical Research Support Program.....					S03s							
				1	103	$ 303						
				2	173	663						
					276	$ 966						
					S07s							
				1	13	$ 226						
				2	503	43,790						
					516	$44,016						
					S08s							
				5	9	$ 713						
					S10s							
				1	23	$ 3,700						
Minority Biomedical Research Support Program..					R13s							
				1	1	$ 75						
					S06s							
				1	1	$ 360						
				2	13	4,053						
				3	14	1,510						
				5	61	18,570						
					89	$24,493 4/						
Office of the Director....										New	2	$ 225
										Mod.	7	970
											9	$1,195 5/
TOTAL		201	$103,561		941	$77,613		12	$ 680		22	$4,875

1/ Includes $ 724 other than Program appropriated funds
2/ Includes $ 30 " " " " "
3/ Includes $ 65 " " " " "
4/ Includes $6,782 " " " " "
5/ Includes $ 695 " " DRR " "

DIVISION OF RESEARCH RESOURCES
FY 82 AWARDS BY COMPONENT
Research, Grants, Research Training, and R&D Contracts



1/ Includes $6.8 million in co-funding arrangements with NEI/NIMH

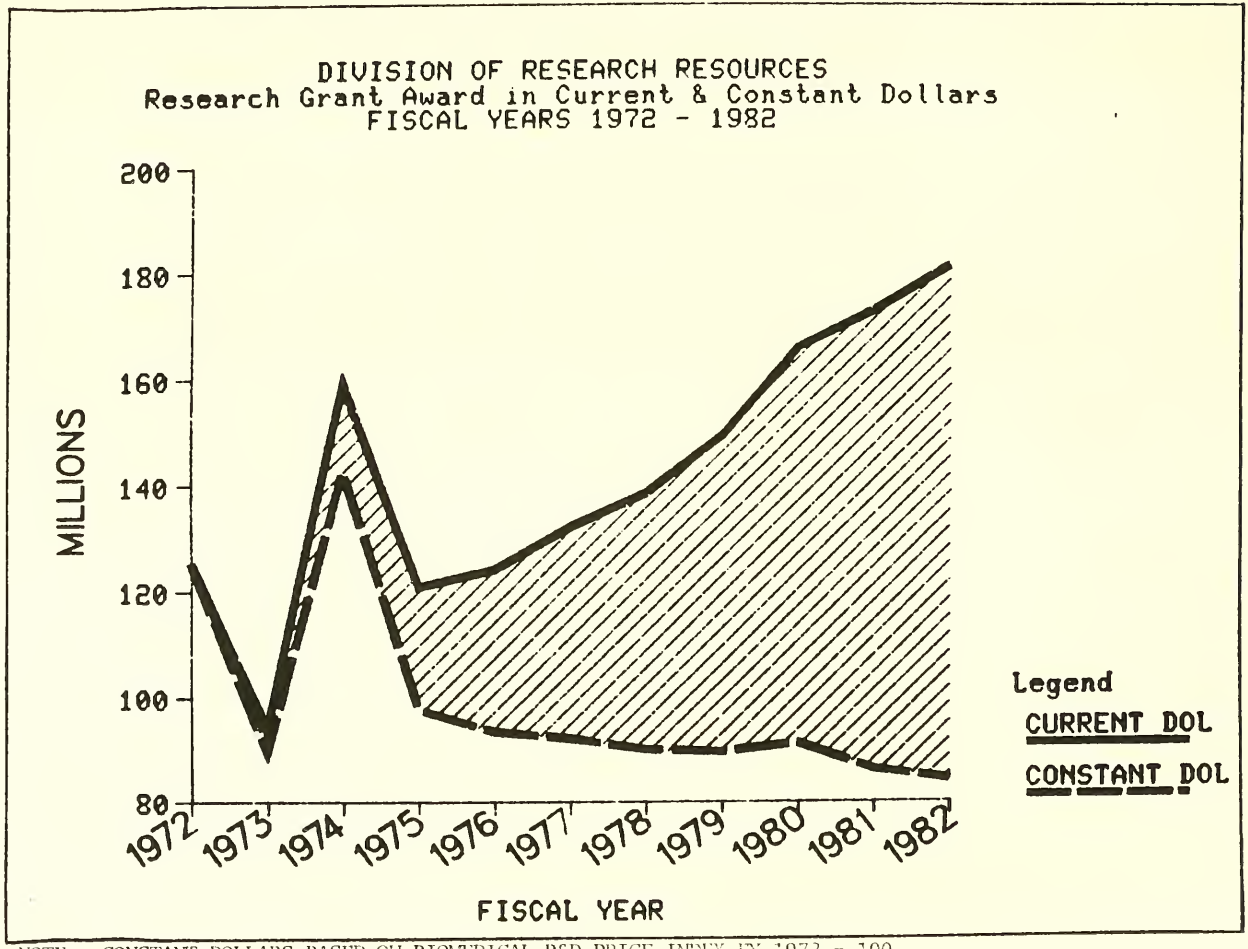
OCCM FY-1982

DIVISION OF RESEARCH RESOURCES

FY 82 AWARDS BY COMPONENT
Research Grants, Research Training, and
R&D Contracts

General Clinical Research Centers Program	Research Centers	$ 63,834,000	
	Other Research	41,000	
	Contracts	24,000	
		$ 63,899,000	(34.2%)
Biotechnology Resources Program	Research Centers	$ 15,326,000	
	Other Research	2,987,000	
	Contracts	3,204,000 1/	
		$ 21,517,000	(11.5%)
Animal Resources Program	Research Centers	$ 24,401,000 2/	
	Other Research	622,000	
	Training	680,000	
	Contracts	452,000	
		$ 26,155,000	(14.0%)
Minority Biomedical Research Support Program	Other Research	$ 24,568,000	(13.2%) 3/
Biomedical Research Support Program	Other Research	$ 49,395,000	(26.5%)
Office of the Director	Contracts	$ 1,195,000	(.6%)
		$186,729,000	(100%)

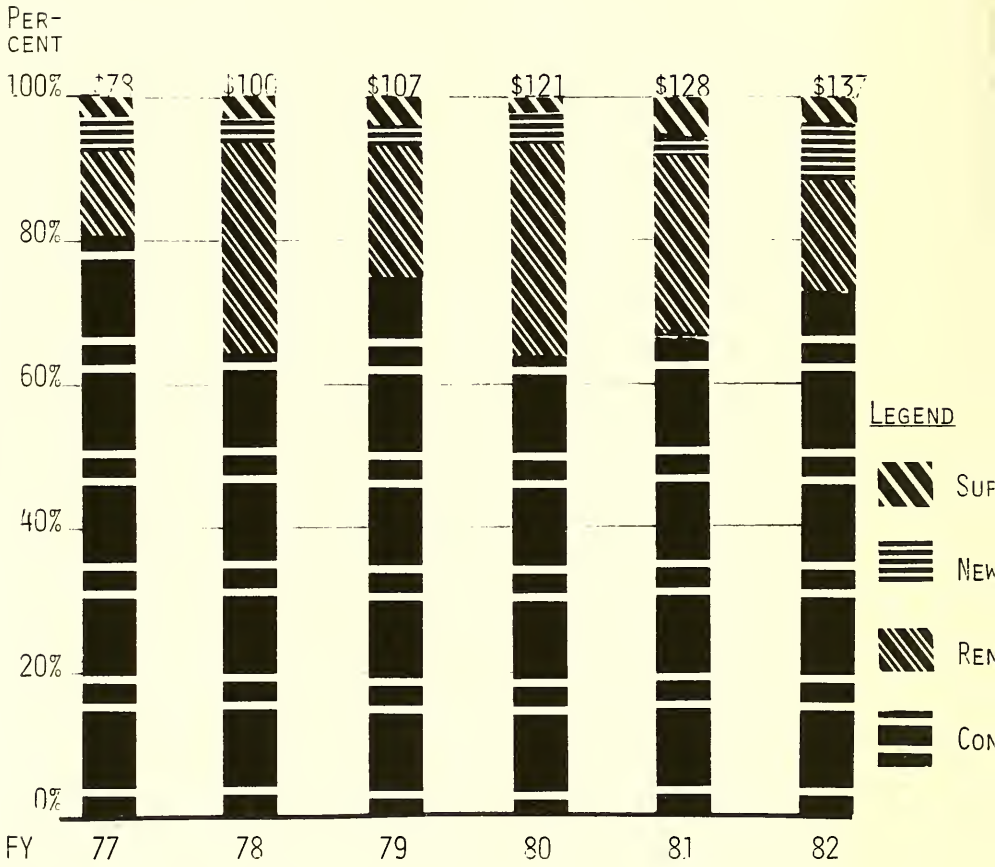
1/ Includes $724,000 in non-FRR funds
2/ $18,399,000 of this amount was for Primate Centers
3/ Includes $6,782,000 in co-funding arrangements with NIH/NIMH



NOTE: CONSTANT DOLLARS BASED ON BIOMEDICAL R&D PRICE INDEX FY 1972 = 100
SOURCE: NIH BASIC DATA BOOKS FY 72-82, NIH, PHS, DHHS; OGCM FY-1982

DRR RESEARCH CENTERS AND OTHER RESEARCH GRANTS BY TYPE
FISCAL YEARS 1977-1982

(PERCENT OF AMOUNT AWARDED; DOLLARS IN MILLIONS)



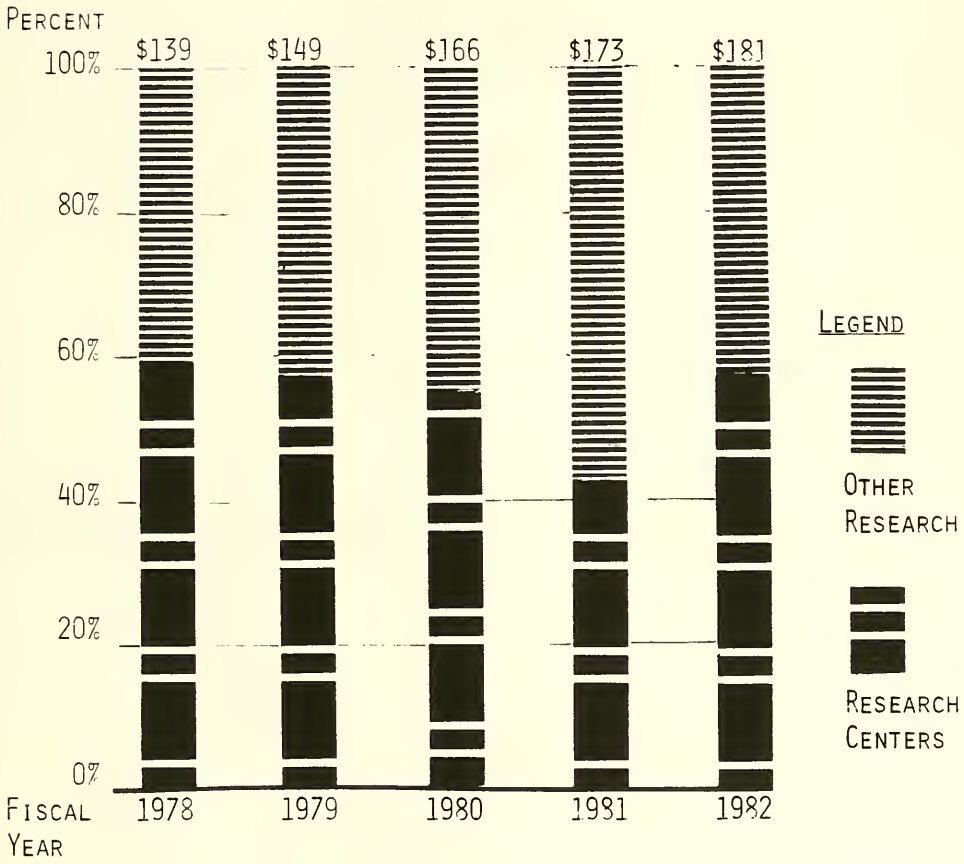
NOTE: EXCLUDES BRS AWARDS

SOURCE 77-81 DATA: NIH, DRG, STATISTICS & ANALYSIS BRANCH

OGCM FY-1982

DISTRIBUTION OF DRR RESEARCH CENTERS AND OTHER RESEARCH GRANTS
Fiscal Years 1978-1982

(Percent of Dollars Awarded)
(In Millions)



Note: Includes BRS Programs
Source 78-81 Data: NIH, DRG, Statistics & Analysis Branch

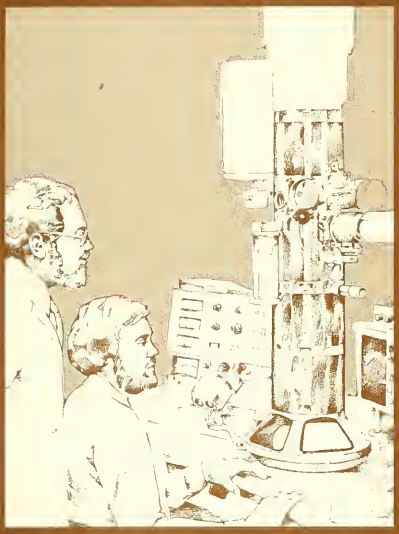
OGCM FY-1982

Division of Research Services

Annual Report

Fiscal Year 1982

National Institutes of Health



The Division of Research Services

The many specialized functions of the Division are designed to support all of the 18 Bureaus, Institutes, and Divisions (BIDs) which constitute the National Institutes of Health. The primary program emphasis, however, is directed at serving the 8,000 staff members of the intramural program, including more than 2,600 doctoral level scientists who conduct research in NIH laboratories.

Organizationally, the Division is structured to provide products and services in support of the sequential steps in every biomedical research project: planning, making available models and substrates, manipulating and measuring research materials, and recording and communicating research results.

- The Library Branch possesses or has access to virtually all published biomedical knowledge to assist the investigator in planning and designing his/her project.
- The Veterinary Resources Branch provides the animal models, organic materials, and proper facilities for their use.
- The Biomedical Engineering and Instrumentation Branch collaborates with the investigator in devising the means whereby research materials may be manipulated and results measured, often with highly sophisticated electronic equipment.
- Finally, the skills of the Medical Arts and Photography Branch are available to all investigators to enable them to record and communicate the results of their research to the scientific community.

Service to NIH Research

Joe R. Held, D.V.M., Director
Division of Research Services
National Institutes of Health

All components of the National Institutes of Health faced a special challenge in Fiscal Year 1982: to keep up the high level of biomedical research performed or funded by NIH while also keeping costs within the limits required by tight budgets.

The management and staff of the Division of Research Services face the same challenge in their task of supplying vital services to NIH's intramural research programs. The following reports of the DRS Branches demonstrates how the Division is following through on its 26-year tradition of service to NIH research. A few introductory highlights from this year's activities might give the flavor of that service:

Biomedical Engineering and Instrumentation Branch

BEIB engineers and instrumentation specialists were particularly pleased this year when Neuro-PET—a vastly improved positron emission tomography scanner—was put into regular clinical use by investigators in the National Institute of Neurological and Communicative Diseases and Stroke (NINCDS). The new scanner, conceived by the NINCDS investigators, is named Neuro-PET for its ability to produce clearer, more precise pictures of the brain than previous PET scanners. BEIB staff in the Electrical Engineering Section, Mechanical Engineering Section, Research Instrumentation Section, and Mechanical Instrumentation Fabrication Section all shared in making NINCDS's improved diagnostic tool possible.

The quality of PET images depends largely on the efficient detection of gamma rays emitted in coincident pairs from the brain of a patient into whose bloodstream radioisotopes have been injected. For Neuro-PET, the NINCDS scientists designed a system of 512 crystal gamma ray detectors (many more than in standard PET scanners) packed tightly into four small-diameter rings.

BEIB engineers designed a sophisticated and complex electronics package for Neuro-PET that can identify coincident pulses from two simultaneous gamma rays among 40,960 possible pairs of detectors, and can code the pulses into numerical data to be transmitted to a computer.

BEIB engineers also designed a gantry to support the rings of detectors and a mechanical system for moving the rings in the desired pattern around the patient's head. These mechanisms were built by BEIB mechanical instrumentation fabricators, who also made valuable suggestions and performed the more detailed designing.

Work on Neuro-PET is not yet complete in NINCDS and BEIB. When it is fully operational, it will produce seven simultaneous brain-slice views, giving even more precision and speedier examinations.

Veterinary Resources Branch

The biomedical research community has become increasingly aware in recent years of the importance of genetic monitoring of inbred laboratory rodents. This awareness has been sharpened recently as journal articles discussed the possible invalidating effect of genetic contamination on research results. For example, a 1982 article in *ILAR News* (Institute of Laboratory Animal Resources) pointed out, "It is high time that all institutions and commercial breeders give serious thought to the development of genetic quality-assurance programs of the sort already implemented by several of the more progressive organizations." The DRS Veterinary Resources Branch inaugurated its Genetics Unit in 1977, both to monitor the genetic integrity of mice and rats maintained by the Branch and to respond to investigators' concerns about animals obtained from contractors. The Unit since then has steadily increased and refined its armamentarium of genetic profiles, using biochemical, immunological, and morphological markers to help investigators ensure the validity and comparability of research results.

Medical Arts and Photography Branch

Though MAPB is primarily engaged in helping researchers graphically record and communicate their findings, the Branch also meets a variety of other NIH information needs. One of their most challenging tasks in FY 1982 was to prepare, on very short notice, 18 exhibits for the White House Conference on Aging. Each exhibit had to focus on one NIH Bureau, Institute, or Division (BID), and illustrate that BID's contributions to improving the health of our nation's elderly. MAPB had the 18 exhibits completed and on display at the conference site when the participants arrived in Washington. But MAPB staff had also seen an opportunity to make double use of the exhibits and thereby help out the NIH components in a time of tight budgets. The Branch designers prepared the exhibits so that, with some modifications, they are now on view in a permanent site—the new NIH Information Center in the Ambulatory Care Research Facility (ACRF).

Library Branch

The NIH Library's portion of this report quite rightly focuses on the automated library services now being installed. But another development this year will also pay off in more efficient service to users: the Library came to grips with the problems of rapidly diminishing space. In the 15 years since the Library moved to its present site, the collection has more than doubled in size. The space crunch became painfully evident when Library staff were intermittently unable to shelve some materials.

One part of the solution is the move to microform. This year the Library accelerated its replacement of backfiles of less-used journals by microfilm versions, and also replaced its bulky collection of telephone books and college catalogs with microfiche.

The other part of the solution is more complex. Working closely with the Library Advisory Committee and other members of the NIH scientific community, the Library is evaluating its entire collection—journals and books—to perform a necessary winnowing without lessening its ability to respond to investigators' needs. The review is being performed in a way designed to give wide notice and review of all proposed removals.

Automated Data Processing in DRS

The large-scale automation of NIH Library services, now under way, is only one part of the Division's continuing increased use of automation to improve output and effectiveness on behalf of NIH intramural research. Growth, innovation, and adjustments in the use of resources are the expressions of an organization geared to meeting the needs of continually evolving research efforts.

In addition to the NIH Library's expanding system, DRS automated data processing systems already in operation include Small Animal Billing, Primate Inventory and Management, and Canine Colony Management in the Veterinary Resources Branch; Design Billing and Graphics Billing in the Medical Arts and Photography Branch; and Scientific Equipment Rental in the Biomedical Engineering and Instrumentation Branch. The Division is planning to purchase additional ADP equipment and software packages during the next five years for use in support of intramural research.

The NIH Library's online catalog and circulation control systems will be in operation around the end of FY 1983, to be followed by other library systems including accounting and management reports, cataloging support, and controls of acquisitions, serial publications, and inventory.

The Small Animal Scientific Data System, to be implemented in the Veterinary Resources Branch over the next five to seven years, will contribute strongly to laboratory animal management by collecting and maintaining comprehensive breeding, genetic, experimental, and environmental data. It will not only provide protocol management for experiments conducted within the DRS facilities, but will also furnish other investigators with fuller information for selecting the best animal models for particular research protocols.

Financial Operations

DRS's original FY 1982 budget authority of $30,891,000 provided for a five percent increase from FY 1981 actual obligations. However, in a continuing effort to initiate cost saving measures, the Division was able to decrease its 1982 requirements by 8.4 percent. Reductions and cost saving methods were examined across the entire Division, with savings primarily in areas financed under the Service and Supply Fund in the Veterinary Resources Branch and the Medical Arts and Photography Branch.

The contract mechanism enabled the Division to adjust services and cost without adversely affecting the NIH. A study on the policies for acquiring commercial or industrial type products and services needed by the Government (OMB Circular A-76) was performed in the Veterinary Resources Branch, resulting in savings of $75,000 from a contract for maintaining a nonhuman primate breeding colony. Another primate breeding colony was sold, eliminating $300,000 obligations. The Medical Arts and Photography Branch initiated a bidding process for jobs going to contractors, insuring the best rate for the government. The current economic situation enhanced the success of this process, which contributed significantly to the $1,018,000 savings.

While faced with the challenge of operating under budget constraints, the Division continued to provide the high quality services to the NIH intramural program and meet increased demands, especially in the repair and maintenance of research instrumentation, primate holding, dog holding, and the purchase of additional equipment for the highly used Scientific Equipment Rental Program. The installation of a total Library automated system continued on schedule.

In the coming year the Division will continue to explore methods to increase productivity, reduce cost, and respond effectively to the NIH scientific community.

Division of Research Services
Annual Budget
(in thousands of dollars)

	FY-81	FY-82	Increase/ Savings
Veterinary Resources	$12,999	$12,534	$ -465
Biomedical Engineering & Instrumentation	8,145	8,460	+315
Library	3,002	3,177	+175
Medical Arts & Photography	5,345	4,327	-1,018
Total	$29,491	$28,498	$ -993

Biomedical Engineering and Instrumentation Branch

Murray Eden, Ph.D., Chief

Engineering and Physical Sciences for NIH Research

A reliable way to measure minute quantities of biologically important elements in tissues has been an elusive need of NIH's research community for many years. The Biomedical Engineering and Instrumentation Branch (BEIB), NIH's central focus of consultative and collaborative support for a wide variety of specialized skills in engineering and the physical sciences, is working to meet that need.

The approach centers upon a 200 KEV analytical electron microscope, specially adapted to produce map-like pictures of the distributions of chemical concentrations within tissues—in addition to the more traditional morphological images. When fully operational, the specially modified microscope will be capable of detecting certain elements in quantities as small as 10^{-20} gram with a spatial resolution under 10 nanometers.

The signals which the microscope produces for analysis are those of the characteristic x-rays and electron energy losses resulting from accelerated electrons interacting with core electrons of the specimen's atoms. In collaboration with the Division of Computer Research and Technology (DCRT), BEIB has interconnected a fast and relatively large "minicomputer" directly to the microscope to acquire these signals and produce the images.

The project's developmental phase is nearing completion, culminating 20 man-years of work over a four year period. Ten man-years have gone into development and modification of the instrumentation. Another ten, the work of the Computer Systems Laboratory, DCRT, have gone into producing the requisite software.

In work with the National Institute of Dental Research, BEIB has already successfully recorded preliminary energy loss images from ameloblasts (enamel-forming cells in the teeth), demonstrating significant amounts of calcium in the secretory granules. Use of such images should help achieve a better understanding of the function of ameloblasts in tooth enamel mineralization.

In other preliminary work with the microscope, measurements on fluorinated biological molecules indicate that some ring compounds (such as neurotransmitters) may be quite stable against radiation damage in the electron beam. BEIB plans to incorporate such substances into cells and to attempt imaging these components with the fluorine label.

In 1982, significant progress has also been made on another major imaging project—NMR imaging for use in medical diagnosis. In particular, BEIB has interconnected the system's spectrometer, pulse programmer, array processor, and computer and has successfully tested several developmental aspects of the system by producing a one-dimensional NMR image. Several other advances will lead to the production of images with information relating to three-dimensional structures.

In collaboration with the Surgical Neurology Branch of the National Institute of Neurology and Communicative Disorders and Stroke, BEIB has made operational an automated image quantification system that can determine the toxicity of chemotherapeutic agents on tumor cells. A concurrent project on an electron microscope has resulted in a five-to ten-fold increase in cell counting speed, as well as substantial improvements in statistical accuracy and numerical consistency. This study is continuing with the goal of improving understanding of brain cancer cell morphology.

The Branch has also been quite busy fulfilling its commitment to provide the NIH research community with a broad range of scientific and engineering expertise. For example, BEIB has collaborated in more than 200 projects to produce advanced instrumentation, models, methods, and techniques dedicated to the acquisition of biomedical information previously unavailable to NIH's scientists.

The staff of 40 professional physical scientists and engineers and 77 technical support personnel responded to over 3,100 requests for the fabrication and modification of laboratory devices and made another 8,600 repairs or minor changes of scientific equipment.

In addition, BEIB and the U.S. Agency for International Development have a continuing agreement in which BEIB provides technical assistance to less developed countries wishing to increase their ability to repair and maintain scientific and medical instrumentation. Currently, BEIB is working closely in this way with the government of Egypt and the governments of several Caribbean nations.

BEIB's professional staff function within four sections and the Office of the Chief. Here is a brief description of their activities in FY 1982:

Applied Clinical Engineering Section (ACES)

This multidisciplinary group, located in the Clinical Center/ACRF complex, provides diversified engineering expertise to a wide variety of collaborative efforts in basic and applied biomedical research. For example, the group is working with the Clinical Pharmacology Branch of the National Cancer Institute to develop a triple-laser flow cytometer that will enhance studies of cancer cell kinetics and hasten the evaluation of chemotherapeutic regimens. The group has also incorporated a PDP 11/34 minicomputer into the system to help the researchers more rapidly acquire and analyze clinical cell samples.

ACES is working in conjunction with Ortec Corporation to develop a concomitant device that will strengthen the results obtained from the flow cytometer. The auxiliary device is a TV-based, microscopic-image analyzer, intended to allow quantification of cellular DNA synthesis. The equipment will use a grain counting technique applicable to specially prepared autoradiographic specimens. ACES's primary contributions were in solving a grain overlay problem and in the analytical treatment of interference introduced by the presence of specific stains bound to the DNA.

Similarly, engineering concepts provided by the section are supporting a flow cytometer used by the National Institutes of Allergy and Infectious Diseases' Laboratory of Parasitic Diseases. The instrument's electronics have been significantly updated, thereby extending its applications. The laboratory is now able to delve more completely into biologic research concerned with the growth mechanisms of intracellular protozoan parasites.

Over the past year, the Laboratory of Animal Surgery of the National Heart, Lung and Blood Institute and the Applied Clinical Engineering Section have worked together to study the physiological principles underlying oscillometry—an old but newly revisited technique for measuring blood pressure indirectly. The method works through analysis of the pulse pattern of pressure changes in a blood pressure cuff during its deflation cycle. Because the technique requires no external transducers and is easy to apply, oscillometry is well suited to indirect measurements of blood pressure in research animals.

On the basis of an *in vitro* oscillometric model and studies using laboratory dogs, the members of the Applied Clinical Engineering Section have identified several underlying principles involving the rheology of arteries and the thermodynamic properties of the cuff. They are currently designing an oscillometric blood pressure system based upon these principles.

Collaboration with the National Heart, Lung and Blood Institute's Surgery Branch has resulted in a heart perfusion circuit that circulates a buffered analog of blood through an isolated heart. This device permits investigation of the heart's biochemical and physiological parameters. The system also allows investigators to induce temporary cardioplegia, during which certain pharmacologic agents can be introduced into the heart. The scientists can then assess the ability of the drugs to maintain cellular life by comparing the heart's pre- and postplegic pumping abilities. This technique may have some utility in stopping and restarting the heart during cardiac surgery and may therefore simplify certain open-heart surgical procedures.

The opening of the Clinical Center's new Ambulatory Care Research Facility (ACRF) led to several new areas of collaborative research for ACES. A completely new speech pathology lab within the ACRF has created a need for specially modified ultrasound equipment to be used in the diagnosis and rehabilitation of certain speech impairments. Similarly, ACES is collaborating with the Diagnostic Radiology Branch of the Clinical Center in developing a miniature, overhead TV camera system to permit precise monitoring of nuclear diagnostic studies during surgical procedures.

ACES is also providing the clinical engineering support necessary for the 500-bed Clinical Center and the Ambulatory Care Research Facility (ACRF). This role evolved from the electrical safety program established for patient care equipment. It consists of programs in the areas of technical standards, medical equipment management, and the training of medical and support staff. An example of this is the section's participation in the formulation and modification of standards affecting patient care.

Chemical Engineering Section (CES)

Historically, chemical engineering developed as a discipline to facilitate the analysis, design, and control of large-scale chemical plants in which intrinsic chemical events are associated with various physical processes such as flow, mixing, and transport. The methodologies of this discipline form a natural and clearly delineated body of science and practice applicable to many biological problems in which physical processes influence biochemical interactions or even dominate them.

The Chemical Engineering Section has pioneered in the development of physiological pharmacokinetics and continues to service as a resource for the design and interpretation of laboratory and clinical studies involving the discipline. Recent work has included the development of pharmacokinetic models for a variety of anticancer drugs, radiation sensitizers, and environmental contaminants. The section has placed particular emphasis on the development of a protocol for the quantitative use of pharmacokinetics in mice and man to improve the effectiveness of Phase I clinical trials. In addition, CES has advanced pharmacokinetic theory through the development of mathematical models, including some for the diffusion of drugs into tissues from body cavities such as the peritoneal or cerebrospinal fluid spaces. These distributed models provide considerable insight into the factors affecting drug absorption and the shape of the concentration profiles in tissues.

A collaboration with the Food and Drug Administration and the American Red Cross, begun during the year, is developing improved techniques for the study of cells in culture. This collaboration builds on the section's past experience with cell culture and synthetic membrane technology, including the application of principles of fluid mechanics and mass transport to the design of new instruments for studying cells under carefully controlled conditions. One instrument permits simultaneous visual and electrical observations fo cultured toad bladder epithelium. A second allows study of the morphology and physiology of arterial endothelial cells exposed to various fluid shear stresses. The devices allow for the regulation of the chemical environment of the cells and can be used to test cellular interactions with well-characterized synthetic support materials.

Analysis of the amino acid sequence of proteins is becoming an increasingly important element in biomedical research. In collaboration with the National Cancer Institute, CES is seeking improved methods for automated sequencing of amino acids. One approach involves the modification of commercially available instruments to enhance the reproducibility and the yield of the sequencing process. The section is also pursuing new technologies to improve techniques for easy, inexpensive, and reliable analysis of very small amounts of proteins and peptides. One new approach involves the use of ultrafiltration membranes that will serve as reaction chamber and separation devices for removing products from reactants in the sequential degradation of the protein.

Development of a fiber-optic sensor for measurements of blood and tissue oxygen pressure has resulted in a working system of probe and associated instrumentation. Evaluation and development for their practical application are under way. The small size, safety, reliability, and low cost of such a probe should provide a significant improvement over currently available methods. The probe is modeled after a similar fiber-optic probe for pH measurement, previously developed in CES and modified and further developed by BEIB's Mechanical Engineering Section for use in physiological experiments. These optical sensors are based on dye-indicator principles with specificity achieved by chemical means.

Segmented polyurethane continues to be an important elastomeric material for applications in surgical implants such as artificial-heart assist pumps, total artificial hearts, and insulation for neuro- and cardiac electrodes. Long term *in vitro* studies, carried out in the CES laboratory for periods up to 13½ years, have elucidated many of the physical characteristics of this polymer when

it is subjected to storage under various wet and dry conditions. Photomicrographic and scanning electron micrographic analyses have disclosed discontinuities in the physical and chemical structure of the polymer that have been attributed to causes arising during synthesis, subsequent handling, and fabrication. These variances may be significant to problems of blood compatibility and surface calcification. CES is also continuing work on the development of special purpose catheters for therapeutic applications. Among these are a balloon catheter for treating bladder tumors with radiation and a miniature flow-directed catheter for interventional radiology.

Electrical and Electronic Engineering Section (EEES)

The Electrical and Electronic Engineering Section continued development of a diverse range of custom instrumentation in support of NIH's intramural research. Despite the severe resource constraints affecting all of NIH, the group was able to increase its effectiveness through increased use of computer-aided design (CAD) and refinement of its interdisciplinary team approach. For example, new staff with expertise in biophysics and electro-optics are complementing the expertise of the section's specialists in electronics, micro-processors, and software.

The fruits of this approach are well exemplified by a new instrument that provides noninvasive measurement of the viability of platelets in transfusion bags. Through CAD, the group developed a sophisticated laser optical measurement technique that extracts the desired parameters by means of a microprocessor-based data handling system. No apparatus to make this important measurement had been developed previously.

A major project in collaboration with the National Institute of Neurological and Communicative Disorders and Stroke is approaching completion. The Neuro-PET scanner is already in regular clinical use, although its ultimate capability of yielding 7 slices is not yet fully implemented. Its electronic circuitry, developed by EEES, has contributed to achieving sensitivity and resolution higher than that of any commercially available instrument. (This project and the noninvasive platelet analyzer have also been supported by BEIB's Mechanical Engineering Section.)

The section has applied considerable effort to a variety of video systems, including some in which the TV camera tube (vidicon) is operated under highly abnormal conditions. A new technique that EEES developed for linearizing vidicon performance under such conditions is being used to good advantage in several spectroscopic applications.

The group also increased its emphasis on bus-oriented instrumentation systems. The expertise of EEES, coupled with the stock of bus-compatible instruments in BEIB's Scientific Equipment Rental Program, provides a unique capability for the rapid and economical development of sophisticated one-of-a-kind instrumentation systems.

A wide variety of other electronic instruments was also developed, ranging from data acquisition systems, controllers, and interfaces to more complex developments such as scanning and de-scanning systems for analytical electron microscopes.

Mechanical Engineering Section (MES)

The Mechanical Engineering Section conducted a wide variety of projects this year involving hardware development, as well as analytical and experimental studies. Several long term projects were brought to fruition, and a number of new initiatives were begun.

Several years of work on a miniature fiber optic pH probe have culminated in the development of a computerized five-channel instrument for measurements in canine myocardium. The National Heart, Lung and Blood Institute uses the instrument extensively as a vital part of several experiments on calcium antagonist drugs. The probe fits inside a ½ mm diameter needle and is extremely rugged and reliable; it is stable and accurate to less than 0.01 pH units. MES has improved the optical design so that an LED can provide the illumination, instead of the previously required tungsten light source driven by a high current stabilized DC supply.

In collaboration with NHLBI, the section has combined a microscope, micromanipulators, and a TV video system to study the mechanical properties of single red blood cell membranes. With this combination, both static deformations and time dependent deformations can be measured under prescribed loads to determine the shear moduli and viscosities of the membranes of normal and diseased red blood cells. MES will use the technique to study sickle cells at various oxygenation levels, and also the red blood cells of diabetics.

The section also developed an analytical continuum model of the left ventricle of the heart to aid in understanding myocardial function. Particular attention was given to the anisotropic effects resulting from the fiber orientations in the heart. The ventricular cycle was analyzed by

specifying the pressures at which the aortic and mitral valves open and close. Ejection fraction and other important parameters are calculated in closed form as functions of variables such as wall thickness, fiber angles, and muscle parameters.

Work continued on the miniature toposcopic catheter that has been under development for several years. The system's reliability and performance have been significantly improved, and clinical use is anticipated in the near future. The outer introducing catheter is number 7 French, and the everting element is 1½ mm in diameter (4.5 French).

During the past year MES has collaboratively collected a large quantity of experimental data on the uptake of fluorescein in tumors, using an *in vivo* fiber optic micro-fluorimetry system developed by members of the section. To analyze data, fast Fourier transform techniques are used to perform deconvolutions which reveal the transport characteristics of the tumors for markers with a range of molecular weights.

Another system being developed in MES is collaboration with the National Heart, Lung and Blood Institute (NHLBI) will allow more precise results in testing drugs used in cardiology. This is a servo pressure feedback control system, designed to control the aortic blood pressure in a dog on a phasic basis. It will eliminate downstream load pressure changes that have heretofore influenced results when the contractility effects of various drugs are being evaluated. Phasic pressure recorded before the drug intervention provides the servo's reference pressure for use after the intervention.

MES is also participating in a long term project with the National Cancer Institute and the Bureau of Radiological Health, FDA, involving the use of microwave radiation to produce localized hyperthermia for treatment of cervical cancer. This involves five steps: characterization of a specially procured microwave antenna system, any necessary modification of the antenna, performance of heat transfer analysis to predict temperature profiles as a function of radiation and perfusion, phantom studies, and collaboration with NCI clinicians to determine doses. If the results justify further elaboration, we will ultimately develop a completely computerized system that would account for factors such as variations in anatomy.

Analytical Methods Group (AMG)

This group within the Office of the Chief collaborates with NIH investigators in three major areas: (1) trace element and complex species characterization and quantitation, (2) mass spectrometry, and (3) analytical ultracentrifugation.

Increasingly sensitive methods of analysis are clarifying the significance of trace elements and their complex species within organisms, especially their relationship to disease processes. This research requires identification, characterization, and quantitation of several elements (for example, copper and gallium) and numerous transition metals (including iron, vanadium, manganese, cobalt, and platinum) and their complex species in biological tissues and fluids. Sensitive analytical techniques are applicable to the study of such things as enzyme inhibitors in affective disorders, enzyme activators in heart disease, the formulation of improved anti-tumor drugs, and pharmacokinetic modeling. As an example, platinum (positively identified by its x-ray energy) is found concentrated in lysosomes of renal cells of rats treated with the antitumor drug cis-Platin. Work is also continuing on development of techniques of administration that minimize the toxic effects of this drug on the kidney. We are doing this by adjusting the proportions of the several chemical forms containing platinum in the drug formulations.

A Secondary Emission Mass Spectrometer (SEMS) system is being assembled to study particle-induce ionization of biological and high molecular weight compounds. The instrument will also serve as a test facility for the development of ion sources and guns for the mass spectrometers used in NIH intramural studies. Other activities have included development of cold emitters for ion sources and modification of mass spectrometers on the NIH campus for application of particle ionization bombardment.

The group has also developed a method of determining the resolving power of low resolution mass spectrometers. Reference compounds used in this method can be used to test the sensitivity of quadrupole mass spectrometers in a high mass range. The group has also built a special quadrupole RF power supply to drive the QUISTOR, which will be studied for possible application in analytical mass spectrometry.

Analytical ultracentrifugation studies have led to collaborative publications on several subjects: the self-association of myoglobin at physiological concentrations, the molecular weight distributions of polysaccharide from *E. coli*, and the thermodynamics of self-association of the C-II protein of phage. Our principal ongoing studies of associating systems are on the stoichiometry and association constants for the binding of plasminogen to fibrinogen.

The group expects to give particular emphasis to investigating the thermodynamics of interaction of various proteins involved in blood clotting in order to identify the interacting molecular regions and their relation to clotting mechanisms.

Scientific Equipment Services (SES)

This group continues to provide scientific equipment design, fabrication, repair and rental services to the NIH scientific community. FY 1982 has brought a noticeable increase in repair requests and a decrease in fabrication requests.

The loss of three highly skilled repair technicians has compounded the effect of the increased repair workload. Because suitable replacements for these personnel have not been available, SES has initiated a formal apprentice program in equipment repair. Three persons are currently enrolled; their training will last between three and four years. During the first year the students are enrolled for 16 hours per week in an electronics technology program at a local school. This training is supplemented by on-the-job training and formal short term courses in other areas, such as refrigeration. To date, we are encouraged with the progress made by the trainees and anticipate that additional trainees will be added when other employees leave and qualified technicians cannot be obtained.

SES management is continually reviewing its operation and attempting to initate changes that will increase its efficiency.

The size of the Scientific Equipment Rental Program and its use by the NIH scientific community are both continuing to grow. During FY 1982 SES purchased an additional $1,500,00 worth of equipment, bringing the value of the equipment in the program to $6,000,000.

Outlook for FY 1983

In the coming year the Applied Clinical Engineering Section expects to continue its support of flow cytometry for both the National Cancer Institute and the National Institute of Arthritis, Diabetes, & Digestive & Kidney Diseases (NIADDKD). The opening of the ACRF is expected to create additional responsibilities for ACES, including assistance in setting up a new speech pathology laboratory.

The efforts of the Clinical Engineering Section in 1983 will be in several areas. One area of continuing emphasis will be pharmacokinetic modeling. Here, projects of direct clinical significance are progressing, including the development of distributed models of both peritoneal and blood-brain transport of numerous anticancer drugs, such as cis-Platin and 5-fluorouracil. An area that is emerging with particular interest is the application of principles of chemical engineering to improvements in instrumentation and techniques of biological measurement. Projects in this area will include development of an implantable fiber optic pH and pO_2 probe, investigation of a novel ultrafiltration-based reactor for protein sequencing, and the design of membrane-based sampling systems for *in vivo* and *in vitro* kinetic studies. CES will also seek more compatible and more durable biomaterials for such implants as heart valves and catheters, and the section expects to apply its previous experiences with hemodynamic studies to new studies of the effects of fluid shear on cultured endothelial cells as these phenomena relate to the development of atherosclerosis.

The Electrical and Electronic Engineering Section plans to emphasize new applications of electro-optical technologies to further developments in the area of bus oriented systems and to support the normal requests for new or modified instrumentation. EEES will also apply considerable effort to completing several major recent projects, including the Neuro-PET, custom electronics for the BEIB electron microscope facility, and the instrument for quantifying platelet viability.

In the Mechanical Engineering Section, a major initiative is beginning in localized hyperthermia, using microwave energy as an adjunct to cancer chemotherapy. The section will also emphasize theoretical biomechanics of soft tissues (e.g., arteries, the myocardium, and other muscles), and experimental studies of the properties of red cell membranes. The toposcopic catheter system will be used clinically, and MES anticipates that numerous laboratories within NIH will use an inexpensive version of the BEIB-developed fiber-optic pH probe. Moreover, novel instrumentation and control for experiments in cardiology that are currently under development (such as phasic aortic pressure control) will receive their first tests.

As developmental work on the instrumentation and software of BEIB's analytical electron microscope comes to a close, the Branch anticipates a number of new collaborations on important biological problems. In analytical methods, BEIB will extend and refine work on the techniques for quantitation and speciation of metal complexes and study their interactions in biological systems. The effort in mass spectrometry will be on testing and evaluation of the equipment and development of data processing methods with application to new systems. In analytical ultracentrifugation further improvements are planned in the data acquisition system with application to thermodynamic measurements on biological macromolecules.

BEIB also expects to have satisfactorily researched and built the basic instrumentation of the NMR imager in 1983 and to have obtained high quality images. More emphasis will be placed on the developing of new NMR imaging techniques with a view to obtaining information on flow, diffusion, and metabolism as well as the more common parameters of relaxation times and proton density. New techniques for displaying the information (involving the use of color) will be under investigation, as will a variety of pulse sequences designed to compensate for inadequacies in field homogeneity.

Medical Arts and Photography Branch

Ronald B. Winterrowd, Chief

Graphic Arts in the Service of Research

Most of the Medical Arts and Photography Branch's work consists of documenting NIH investigators' scientific data through photographs and graphic illustrations for publication in journals or for presentation at scientific or lay meetings. MAPB also supplies various other NIH information needs.

The last ten years have seen an annual increase of from 10 to 20 percent in the Branch's graphic art services provided to the NIH community. In FY 1982, for the first time, the demand for these services did not rise, and in some sections it decreased. Inflation, budget constraints, and a moratorium on the printing of Federal publications contributed to the lessened demand. Fortunately, the large increases of the past several years were managed through an increased use of contractors, so it has been possible to absorb the current decreases without disrupting the inhouse program.

The Branch's staff of 49 artists, photographers, and other specialists has extensive expertise in converting data into effective presentations. They are highly skilled in meeting the needs of scientists for graphic presentation, medical arts, and still and motion picture photography, including photomacrography and photomicrography. Services include design and production of publications; preparation of slides, vugraphs, and other projected visual aids; animation artwork; technical, general, and medical illustrations; exhibit design; statistical drafting; display charts; posters; and medical models.

The philosophy of the Branch is to provide high quality professional services competitive in cost with commercially obtainable services. On contracted work, the staff works closely with vendors of graphic and photographic services to ensure that MAPB's quality standards are kept.

To reduce users' costs while maintaining productivity and product quality, MAPB has set up an educational program on cost awareness and cost reduction within the NIH community. It stresses the savings in money and time that investigators can derive by thinking through in advance how they want their articles and presentations illustrated, discussing their requirements with MAPB at an early stage, and adhering to their plan once it has been made.

Investigators are advised to submit complete, clear, and accurate raw data for display as early as possible. Careful planning can eliminate two causes of expense: 24-hour rush service to meet a deadline, and changes in artwork that has been prepared in final form. Rush service costs 50 to 100 percent more than regular, and changes or corrections on final artwork can double its cost.

Staff members also ask investigators to order only the necessary number of slides and pictures, and tell how to protect artwork for future reprinting; replacement of damaged materials can be as costly as the original.

In another effort to contain costs, the Graphics Unit requires bids on all contract work, even through procurement regulations require negotiations only for bids over $500.00. This procedure has realized savings of approximately 25 percent.

Photography Section

The Photography Section's requests for services dropped by 9 percent during the year. Photography support services in photomicrography, photomacrography laboratory work, and technical information were provided to NIH investigators by highly trained photography technicians using advanced printing and processing equipment. To supplement our inhouse facilities, the section continued to obtain the services of vendors in the Washington, D.C., area.

Motion Picture Section

The number of filming requests was about the same as in 1981, with several more formal productions completed than in the previous year.

Design/Graphics Section

As a result of budget limitations and the moratorium on printing, the workload of the Design and Graphics Units decreased by 18 and 12 percent, respectively. Despite restrictions on costs, the sections' quality and performance standards remained high. This section, capable of filling requests for complex visual productions, received several awards during the year.

Medical Illustration Section

This section is staffed with talented, highly trained artists who possess a broad background in medical science. Their workload remained constant, with a trend toward surgical illustrations for journal articles and other scientific papers, slides, medical atlases, and other longer-term projects.

Outlook for FY 1983

Tight budgets will probably continue to hold down requests for the Branch's services. Because MAPB provides the vital function of recording and communicating the research findings of the NIH biomedical community, the Branch plans to continue aggressively finding and using new ways to reduce costs and improve services. The educational program to inform MAPB's clients how best to achieve their objectives will be continued.

Veterinary Resources Branch

Robert A. Whitney, D.V.M., Chief

Laboratory Animal Science—A Full Range of Services

The Veterinary Resources Branch (VRB) provides the NIH intramural research programs with a wide range of professional and technical services:

- Production of defined research animals
- Procurement, quarantine, conditioning, and issuance of animals from outside sources
- Management of a central animal surgery and radiology facility
- Animal disease diagnosis and control
- Genetic monitoring of defined research animals
- Research holding for primates, cats, dogs, and livestock
- Consultative services on animal health, care, husbandry, genetics, and nutrition.

VRB also maintains the NIH Animal Genetic Resource and provides administrative support for the Interagency Primate Steering Committee.

During FY 1982 the demand for research animals decreased somewhat, and one of VRB's major emphases has been to adjust the balance between supply and demand and to hold down costs.

The Branch's role as a public information source was intensified because of a high level of public interest in laboratory animals. By request of a Maryland court, VRB provided long-term care for several monkeys pending the outcome of trials and appeals concerning the maintenance of these research animals at a grantee institution. In addition, VRB staff members have been active on several NIH committees formed to address issues of animal care in intramural and extramural programs.

Animal Center Section

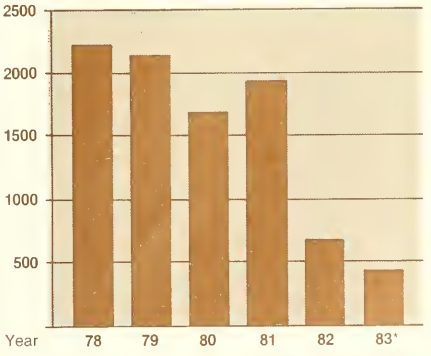
The NIH Animal Center in Poolesville, Maryland, produces and maintains large laboratory animals and provides related services and products for NIH investigators.

The Primate Quarantine Unit procures and quarantines nonhuman primates, manages contract breeding programs, and provides long-term holding of primates for NIH intramural research components and some other Federal research organizations.

The number of rhesus and cynomolgus monkeys issued has declined markedly, largely because of reduced requirements of the National Center for Drugs and Biologics (NCDB) of the Food and Drug Administration (Figure 1). On the other hand, research requiring monkeys has become more long-term in nature, and the Center's facilities are increasingly used to provide extended holding of primates for various institutes (Figure 2). In addition, one contract production program was terminated and the production level of another was reduced to avoid generating surplus rhesus monkeys. An interagency agreement was implemented to produce tamarins (Saquinus mystax) for NCDB research programs.

Livestock populations maintained by the Ungulate Unit remained stable (Figure 3), although the use of blood and blood products declined slightly. A herd of 225 miniature swine is maintained for the National Cancer Institute as a resource for studies in transportation immunology. In addition, stock was provided to a contractor to supplement production by the Animal Center. The National Heart, Lung, and Blood Institute increased its use of sheep for

Figure 1.
Total Nonhuman Primates Issued



surgical research, resulting in a greater demand for sheep blood and a greater number of sheep held pre- and postoperatively.

In the Carnivore Unit, programs are being modified to reflect marked curtailments in the demand for cats, foxhounds, and canine blood. Colony sizes have been reduced, and space is being converted to meet increased long-term holding requirements and to produce defined beagles for the National Cancer Institute (Figures 4 and 5).

Small Animal Section

The Small Animal Section provides rodents and rabbits from its production colonies and also manages contracts for this purpose. It manages the NIH Animal Genetic Resource, containing more than 200 defined strains, and has programs devoted to animal model development, nutrition, and health.

Approximately 230,000 animals were issued from the sections' colonies, a decline of 50,000 from last year, while the number obtained from contract sources was stable at 610,000 (Figure 6). The reduction was related to a decreased demand by NIH investigators and the need to halt production of some stocks and strains contaminated with mouse hepatitis virus until one autoclave was repaired. No new contracts for the purchase

Figure 2.
Nonhuman Primate Holding Days

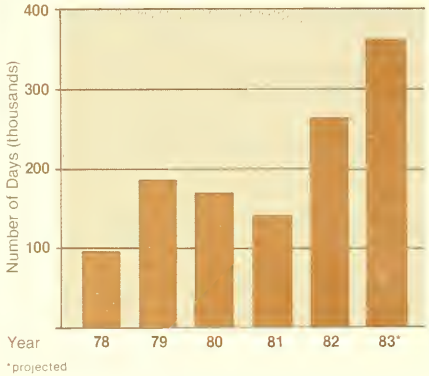


Figure 3.
Livestock Holding Days

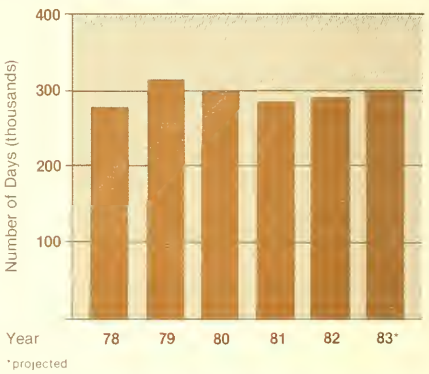


Figure 4.
Foxhounds and Beagles Issued

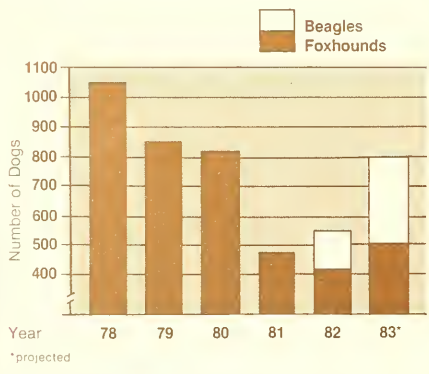
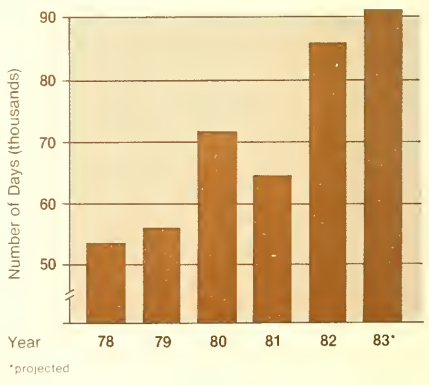


Figure 5.
Long-term Dog Holding



of small animals from commercial breeders were issued during the year.

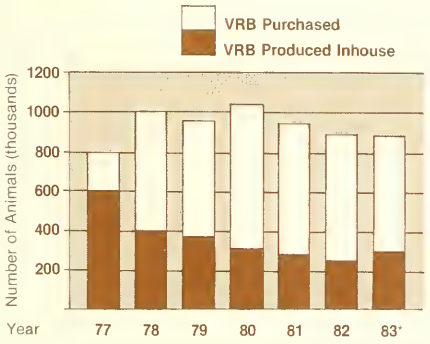
Because of investigators' concern with the potential effects of diet on experimental results, many of them requested nutritional information or modifications in diet formulations to accommodate specific program requirements. The program to monitor diets for various chemical contaminants continues, but there is no indication so far that contaminants are a problem when diets are manufactured in facilities that meet NIH contract requirements.

The development of new open formula diets continues, with emphasis on a nonhuman primate diet and a rodent diet formulated specifically for use in toxicology studies. The nonhuman primate diet has been evaluated in various colonies and will apparently soon replace the closed formula diet currently purchased by sole-source contract. A price evaluation showed that open formula diets purchased through advertised contracts cost the NIH about 38 percent less than closed formula diets purchased as sole-source items. It is estimated the NIH will save about $80,000 this year by using open formula diets.

Extensive studies have been undertaken in collaboration with the National Heart, Lung, and Blood Institute and the National Eye Institute to ascertain the effects of dietary constituents on the incidence of stroke in the stroke-prone rat and the incidence of cataracts in PETH and RCS rats.

Renovations completed in July will allow VRB, for the first time, to offer a rodent holding service for NIH investigators. The renovated facilities will be used initially to hold animals for the National Institute of Allergy and Infectious Diseases until renovations of that institute's facilities are completed.

Figure 6.
Small Animals Issued



Comparative Pathology Section

The Comparative Pathology Section is responsible for monitoring the health status of laboratory animals produced, quarantined, or used at the NIH. It studies the naturally occurring diseases of these animals and developes measures to improve their health. The section also ensures the genetic quality of animals produced by VRB either for use by NIH programs or to be sent throughout the world from the NIH Animal Genetic Resource.

The Pathology Unit intensified its routine monitoring this year, and also responded to an outbreak of mouse hepatitis virus in the barrier-maintained colonies. Many other necropsies were performed to assist NIH investigators in distinguishing naturally occurring diseases from experimentally induced conditions. All these factors caused a 28 percent increase in the number of necropsies performed by the Unit.

Changes in methods used to monitor animal health have improved efficiency and resulted in a 17 percent decrease in the number of samples required. The number of samples processed by the Microbiology Unit increased slightly, however, because of a greater need for microbiologic investigations in connection with diagnostic pathology.

Intramural researchers' use of the Animal Disease Investigation Service declined by 13 percent during the year; the decrease is thought to reflect overall reductions in the use of laboratory animals.

Genetic monitoring of inbred mice and rats from the colonies of the NIH Animal Genetic Resource increased: rodents monitored from the foundation colony increased in number from 758 to 808, and in the pedigreed expansion colony from 62 to 143. Genetic contamination was found in a VRB foundation colony of BALB/c nude congenic mice (BALB/cAnN-*nu*), but no animals have ever been issued from this colony. Back-crossing is under way in the Small Animal Section to make this congenic strain available from VRB. The Genetics Unit also conducted two major investigations of genetic contamination in inbred mice received from contractors. The number of requests from NIH components for investigations of genetic problems was stable at 25.

Veterinary Medicine and Surgery Section

The professional staff of the Veterinary Medicine and Surgery Section interacts with NIH investigators in defining and developing animal models to best meet intramural research program needs. During the past year, the section assisted in implementing 23 new studies involving its animals and facilities.

The Surgery Unit provides central animal radiological and surgical facilities to NIH investigators. The Comparative Medicine Unit works closely with the surgical staff both to provide comprehensive veterinary services for the care of animals and to meet research protocol needs.

The Primate Research Unit provides research holding for more than 1200 nonhuman primates assigned to investigators representing most of the NIH institutes. The demand for central holding space remained high, and the section is continuing to issue animals from one study to another through its primate recycle program—a cost-saving feature as well as an effort to conserve nonhuman primates.

Timed-pregnant primates are used by the National Institute of Child Health and Human Development and the National Institute of Neurological and Communicative Diseases and Stroke for studies in a number of areas include birth defects and fetal effects of infectious diseases. Investigators used fewer timed-pregnant primates this year because of program changes in the institutes, resulting primarily from budget restrictions. The section terminated the contract source of these animals and can now meet investigators' needs from its inhouse colony of timed-pregnant rhesus and cynomolgus monkeys.

Interagency Primate Steering Committee

The Interagency Primate Steering Committee (IPSC) prepared a report updating the National Primate Plan, which was published in 1978. The IPSC represents the combined interests of Federal agencies in the supply, use, and conservation of nonhuman primates for many essential health activities, especially biomedical research and testing. The National Primate Plan was prepared to ensure adequate supplies of these irreplaceable animals.

The new report reviews current requirements for nonhuman primates to meet health needs. Regarding importation and domestic breeding, it makes specific recommendations which reflect the overall decline in the use of these species. The reduced utilization appears to result from increasing costs for animals, budgetary constraints, the substitution of other species or methods, and the application of recommendations in the National Primate Plan to use these animals only when necessary and then in the most effective manner, including sharing among users.

The IPSC also sponsored a task force meeting to develop recommendations for preserving and maintaining chimpanzees used in research, and it has supported the development of a handbook, *Behavior and Management of Chimpanzees in Captivity*.

Programs to assist interested Latin American, Asian, and African countries in the breeding and conservation of indigenous species were continued through the Pan American Health Organization (PAHO) and the World Health Organization (WHO). The Committee also reviewed a draft convention of the Council of Europe on the protection of experimental animals and drafted the Federal Government's response to an inquiry from the Council about the possibility of the United States becoming a signatory to the convention.

Guidelines for the transportation of nonhuman primates were developed by the IPSC and recommended for adoption by Federal agencies and other organizations that need to transport these animals.

Outlook for 1983

The automated data processing system at the Animal Center will be expanded to include the capability to bill users for animals, products, and services. The lease arrangement for the Three Springs Farm, adjoining the Center, will be terminated.

The use of VRB-produced rodents is expected to increase when the Branch begins holding rodents for investigators from the National Institute of Allergy and Infectious Diseases in the recently renovated facilities in Building 14B; VRB will establish production colonies to meet these investigators' needs. In addition, many stocks and strains will be reintroduced into the barrier area to replace those that were eliminated last year to control an outbreak of mouse hepatitis virus.

The Interagency Primate Steering Committee will continue to monitor utilization of nonhuman primates and develop recommendations for meeting biomedical research needs.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Library Branch

Carolyn Brown, Chief

Coming—A Fully Automated Library System

To improve users' access to materials, the NIH Library has continued to move toward automation of all routine functions, building on the groundwork of the automated bibliographic search system and circulation control system already in place. The completed data base will reflect the Library's total holdings.

Construction of a computer room to house the new automated library system began as this fiscal year ended. Delivery of the computer is expected by April 1983. In preparation, the conversion of the Library catalog to machine-readable form was two-thirds completed at the end of the year. Files should be loaded and the online catalog activated during FY 1983. Journal control and other services will follow, including improvements in our automated circulation controls.

When the system has been installed, users will be able to browse the online catalog with touch-screen terminals similar to those used at automated banking stations. By touching various squares on the screen, the user can search the catalog by author, title, or call number. Within seconds, the screen will display the bibliographic description of any item in the collection, plus the location and circulation status of any copy of that item.

The information about each item's status will be current because the circulation control system updates the online catalog the instant it processes each loan. Online circulation control will also eliminate the current one-day delay before a change in a book's circulation status is recorded on computer, and a backup microcomputer will continue to record checkouts and returns if the main computer is temporarily down. Transactions will be recorded by the very reliable bar code system used at automated grocery checkout counters.

Another improvement in the Library's journal control system was already made this year. Information about journals received is now entered online into the PHILSOM system (Periodical Holdings in Libraries of Schools of Medicine), a data base of journal information from a network of 19 medical libraries, including the NIH Library. The new online system can provide, on demand, lists of the Library's daily receipts, complete holdings, and skipped issues claimable from the publisher.

Yet another new online service for users in 1982 was access to the Library's Monthly Acquisitions List, now available through WYLBUR, the computer system maintained by the NIH Division of Computer Research and Technology. Regular printed copies of the monthly list continue to be available to the Library's users as well.

Computerized Bibliographic Retrieval Services

Another of the Library's automated services—computerized bibliographic retrieval—continued to occupy a high percentage of the workload in the Reference and Bibliographic Services Section. As prices rose for searching many of the online files, it became necessary to reduce searches of the pre-1975 literature; most investigators were satisfied by citations from the more current literature. The number of searches remained approximately constant because of almost level funding and a careful effort to conserve funds.

A study of users' satisfaction with the Library's online search services was made this year by a student in the University of Maryland's Graduate School of Library and Information Services. The staff was happy to learn that 87 percent of the 295 respondents in the survey rated the search interview "very satisfactory," and 88.3 percent judged the search results to be either "of major value" or "of considerable value." Many of the respondents also praised the turn-around time.

Journals and Books—Solving the Space Problem

The growth of the NIH Library's holdings through the years has resulted in insufficient shelf space. As lack of space became acute, the Library began weeding the 6,000 titles in the journal collection, starting with a review of 900 journals that have either ceased publication or been discontinued by the Library. This year the weeding of the journal collection continued, and a similar review of the book collection was begun. The selection and review of material proposed for removal from the shelves has involved all sections of the Library as well as the Library Advisory Committee and interested NIH staff. The project will continue throughout FY 1983.

The Library's actions to relieve space problems were hampered somewhat by the Government-wide freeze on hiring, which caused lengthy vacancies in several positions most involved in decisions on removing material from the collection. Among these vacancies were the positions of Library Chief, Deputy Chief, and Section Chief for Reference and Bibliographic Services.

Readers Services Section

In a continuing effort to upgrade and update the Library's photocopying facilities, the Readers Services Section has replaced older equipment with newer machines, after placing several trial models in our user area and obtaining users' comments on them.

Services of the NIH Library

The NIH Library offers a full array of services to assist scientific investigators in their work. They include:

- **Computer Bibliographic Services** - Six specialists perform computerized literature searches and compile bibliographics upon request. The staff is experienced in retrieving citations and abstracts from some 155 scientific data bases.
- **Current Awareness Service** - The Library's Selective Dissemination of Information (SDI) program provides users with regular computer updates on new literature in any specified subject area.
- **Reference Services** - Reference librarians not only answer reference questions on site or by telephone (496-2184), but also advise users of other library services that may meet their needs.
- **Photocopying** - High speed photocopying machines are available to users. The Library also fulfills copying requests.
- **Microfilm and Microfiche** - Many journals are also kept in microform. Most are backfiles of important titles, acquired in order to save space. Reader-printers are located nearby.
- **Circulation** - Books other than reference works can be checked out. Second copies of certain journals are also available for circulation.
- **Interlibrary Loans** - Research publications not in the collection can be obtained from other libraries. Photocopies of journal articles obtained from the National Library of Medicine are usually provided in one to three workdays.
- **Translations** - Foreign language scientific materials are translated at request, and the translations are made available to other users as well.
- **Stack Service** - Library staff will search for any volume a user cannot find on the shelves.
- **Monthly Acquisitions List** - This list, "Recent Additions to the NIH Library," is available in printed form and on the NIH WYLBUR computer system.
- **Library Tours** - A tour with explanations of NIH Library services and policies is available every Wednesday at 2 p.m.
- **Carrels** - Private study carrels are available on limited, first-come basis.